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Maternal Life Course Adversity: The Intersection of Psychosocial and Biobehavioral Adaptive Response in Pregnancy

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MATERNAL LIFE COURSE ADVERSITY:

THE INTERSECTION OF PSYCHOSOCIAL AND BIOBEHAVIORAL ADAPTIVE RESPONSE IN PREGNANCY

By

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DEDICATION

This dissertation is dedicated to my daughters

Nina & Josie

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ABSTRACT

MATERNAL LIFE COURSE ADVERSITY: THE INTERSECTION OF PSYCHOSOCIAL AND BIOBEHAVIORAL ADAPTIVE RESPONSE IN PREGNANCY

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The link between life course adversity and adverse health outcomes is well established, particularly early life adversity (ELA). There is also evidence that the physiologic adaptations associated with stress, depression and ELA can be transmitted intergenerationally via long-term set-point changes within the maternal hypothalamic-pituitary-adrenal axis (HPA). It is unknown how the type and timing of maternal stress and adversity influences HPA regulation during pregnancy and whether maternal coping attenuates this relationship. Manuscript 1 was an integrative review of studies examining the association between maternal ELA and HPA regulation during pregnancy. In manuscripts 2 and 3 the findings of the dissertation study are presented. The purpose of this dissertation was to further examine how the type and timing of maternal adversity is linked to physiologic HPA adaptations in pregnancy and whether psychosocial processes moderate the relationship between life adversity and HPA regulation. From a qualitative perspective, this study examined how situational factors in women's lives influence their goals, motivations, and notions of health in pregnancy. The sample (N = 72) included women in the 2nd trimester of a singleton, uncomplicated pregnancy. The data collected included surveys, interviews, and salivary cortisol samples. Quantitative data were analyzed using correlation and general linear modeling. Lifetime stress was significantly correlated with higher cortisol during pregnancy. Childhood adversity accounted for cortisol elevations in the morning, while adult stress and depression accounted for elevated cortisol

levels in the evening. Women's willingness to seek social support significantly attenuated HPA reactivity. Neither stress nor cortisol were associated with birth outcomes. The qualitative study found that contextual and sociodemographic factors have a profound influence on the way that women prioritize life goals and health during pregnancy. Overall, women's experience of adversity throughout the life course results in specific psychosocial and biobehavioral adaptive responses that shape the gestational environment and pregnancy experience.

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LIST OF ABBREVIATIONS

11β-HSD	11 beta-hydroxysteroid dehydrogenase type 2
ACES	adverse childhood events survey
ACTH	adrenocorticotrophin releasing hormone
APA	American Psychological Association
AUCg	area under the curve with respect to ground
CA	child abuse
CAR	cortisol awakening response
CDC	Centers for Disease Control
CRH	corticotrophin releasing hormone
CRP	C reactive protein
CSA	childhood sexual abuse
CTQ	Childhood Trauma Questionnaire
DHEA	dehydroepiandrosterone
ELA	early life adversity
EMA	ecological momentary assessment
EPDS	Edinburgh Postnatal Depression Scale
GA	gestational age
HPA	hypothalamic-pituitary-adrenal
HPQ-II	Health Practices in Pregnancy Questionnaire-II
IL-6	interleukin 6
IOM	Institute of Medicine
IPV	intimate partner violence
PA	physical abuse
STRAIN	Stress and Adversity Inventory
TM	trimester

INTRODUCTION

Pregnancy is a critical period in human development and is one of the earliest points of preventative intervention in the human lifespan (Halfon & Hochstein, 2002). Characteristics of the intra-uterine environment are influenced by both maternal health behaviors (Ojha, Fainberg, Sebert, Budge, & Symonds, 2015) and maternal physiologic responses to stress (Entringer et al., 2012). These early environmental influences affect risk for disease later in childhood and adulthood (Entringer et al., 2012). A report by the Institute of Medicine (IOM) (2015) highlighted the role of maternal stress and nutrition prior to and during pregnancy as important determinants of childhood health outcomes such as obesity. Additionally, numerous objectives within Healthy People 2020 focus on improving birth outcomes (reduce low birth weight and preterm birth) and health behaviors during pregnancy (increase early and adequate prenatal care, increase abstinence from alcohol, cigarettes and illicit drugs during pregnancy) (US Dept. of Health and Human Services, 2015). Pregnancy is an ideal time to deliver interventions that promote positive health behaviors in women, which can reduce the risk for adverse birth outcomes and disease later in life. Despite efforts to implement health promotion interventions in prenatal care settings, behavior-related pregnancy complications continue to rise, such as excessive weight gain, gestational diabetes, hypertension and preterm birth (Blencowe et al., 2012; Hutcheon, Lisonkova, & Joseph, 2011; Yaktine & Rasmussen, 2009). Understanding the role of stress and coping in relation to maternal behaviors and physiology may provide new directions for effective health behavior intervention research for pregnant women.

The study is guided by life course theory (Elder, Johnson, & Crosnoe, 2003; Halfon & Hochstein, 2002) which emphasize the role of risk and protective factors on an individual's long-term health and disease trajectory via transactions that occur between environmental contexts and bio-behavioral regulatory systems. Within maternal-child health, a woman's cumulative

experience of stress and adversity over the life course becomes biologically embedded to influence important regulatory systems during pregnancy. Biological embedding is defined as a process in which early life experience leads to long-lasting biological alterations that may go on to affect adult health outcomes, including reproductive health (Nist, 2017).

Lifetime Stress and Adversity

Stress prior to and during pregnancy is associated with adverse infant and childhood outcomes, including preterm birth, low birth weight impaired cognitive development, and childhood behavioral and mental health disorders (Betts, Williams, Najman, Scott, & Alati, 2014; Class, Lichtenstein, Langstrom, & D'Onofrio, 2011; Khashan et al., 2011; Kleinhaus et al., 2013; Lamb et al., 2014). These outcomes are mediated by complex behavioral and physiologic pathways. From a behavioral perspective, stress diminishes women's engagement in positive health behaviors during pregnancy, with stress being one of the most consistent and strongest predictors of unhealthy lifestyle (sedentariness, overeating, substance use, smoking) and poor health (APA, 2014; Kratz & Vaughan, 2012). Among women with high levels of perceived stress, 40% say they eat to manage stress, 21% say they drink alcohol and 19% report smoking to manage stress (American Psychological Association [APA], 2014). Furthermore, from a physiologic perspective, stress affects the regulation of cortisol, a hormone highly involved in placental physiology, fetal development and timing of parturition (Braun, Challis, Newnham, & Sloboda, 2013; Buss et al., 2009).

Hypothalamic Pituitary Adrenal Axis

The pattern of cortisol in pregnancy maintains a diurnal rhythm, peaking in the morning after awakening, and gradually decreasing over the course of the day (Entringer et al., 2010). Pregnancy is also associated with two unique cortisol dynamics, including a 3-fold increase over

the course of gestation and a progressive flattening of the morning response (Entringer et al., 2010; Hellgren, Åkerud, Skalkidou, & Sundström-Poromaa, 2013; Jung et al., 2011). Evidence suggests that dysregulated patterns of cortisol regulation in pregnant women may be represented by a lack of normal morning attenuation of the cortisol awakening response (CAR) by late pregnancy, increased total cortisol output (area under the curve [AUC]), and flatter morning-evening slope.

Cortisol dysregulation is associated with maternal distress, shorter gestation, restriction of fetal growth, and later childhood health outcomes such overweight and affective problems (Buss, Entringer, & Wadhwa, 2012; S Entringer, Buss, Andersen, Chicz-DeMet, & Wadhwa, 2011; Hohwü et al., 2015; Hompes et al., 2012). Furthermore, dimensions of stress, such as timing, duration, severity and characteristic may have specific impacts on these dysregulated cortisol patterns and birth outcomes. For example, evidence suggests that timing of stress, in the form of childhood adversity, is associated with higher CAR in late pregnancy and higher evening cortisol levels (Bublitz & Stroud, 2012). Abused pregnant women have also shown altered cardiac vasovagal response to challenge, higher incidence of infections during pregnancy, higher incidence of postpartum depression, and have infants with altered cortisol response to a heel-stick procedure (Records & Rice, 2009; Rice & Records, 2006, 2008; Winn, Records, & Rice, 2003) There is some evidence that these HPA dysregulation can be buffered by supportive social environments (Bublitz, Parade, & Stroud, 2014; Mustoe, Taylor, Birnie, Huffman, & French, 2014).

Chronic stress, such as poor neighborhood quality, crime, racial discrimination and poverty affect Black women disproportionately compared to White women, and may help to explain racial disparities in birth outcomes, such as preterm birth (Giurgescu et al., 2012; O'Campo et

al., 2008). Perceived pregnancy specific stress has also been linked to higher cortisol levels (Kane, Schetter, Glynn, Hobel, & Sandman, 2014).

Few studies have comprehensively examined the multiple dimensions of lifetime stress in relation to cortisol among pregnant women. Therefore, this study will examine in further detail the relationship between dimensions of lifetime stress such as the timing, duration, severity and characteristic of stress in relation to cortisol regulation during pregnancy.

Coping

Coping is defined as "constantly changing cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person" (Lazarus & Folkman, 1984, p. 141). The Brief COPE (Carver, 1997) distinguishes between 14 coping strategies. In the context of pregnancy, an active coping style involves the use of strategies such as emotional support, positive reframing, planning, humor, acceptance and religion (Ruiz et al., 2015). It has been associated with less distress, better prenatal care and less weight gain during pregnancy (Morling, Kitayama, & Miyamoto, 2003). Disengaged coping, on the other hand, involves strategies such as denial and behavioral disengagement (Ruiz et al., 2015) it has been associated with greater prenatal distress (Yali & Lobel, 2002) and anxiety (Hamilton & Lobel, 2008), higher levels of the hormone corticotrophin-releasing hormone (Latendresse & Ruiz, 2011), and preterm birth (Dole et al., 2004). To date, few studies have examined the effect of coping on physiologic stress biomarkers during pregnancy, only one of which examined cortisol (Harville, Savitz, Dole, Herring, & Thorp, 2009). Although this large population study did not find significant correlations between cortisol and stress or coping, it was methodologically limited with the use of a one-time cortisol sample collection. One-time sampling methods have shown poor correlations ($r < 0.1$) with gold-

standard measures of cortisol (Harville et al., 2007), and this limited the ability to detect a difference. To our knowledge, no studies have examined the moderating role of coping styles on health behaviors, cortisol and birth outcomes in pregnancy (see review by Guardino & Dunkel Schetter, 2014).

Health Behaviors

Health behaviors during pregnancy include eating a balanced diet, exercising, avoiding harmful substances, and utilizing prenatal care. During pregnancy, women are often motivated to engage in these health behaviors to achieve positive birth outcomes (Paul, Graham, & Olson, 2013). However, they may struggle to do so because certain behaviors such as excessive eating, smoking and drinking have become a primary means for coping with stress and adverse life circumstances (APA, 2014). Despite efforts to educate pregnant women about the benefits of positive health behaviors, rates of follow-through with these recommendations remain stagnant. Specifically, rates of overweight, obesity and excessive weight gain during pregnancy have reached an all-time high (Yaktine & Rasmussen, 2009) and rates of smoking during pregnancy have changed little over the last couple decades (Ebrahim, Floyd, Merritt II, Decoufle, & Holtzman, 2000; Swamy, Reddick, Brouwer, Pollak, & Myers, 2011; Tong, Dietz, Farr, D'Angelo, & England, 2013). Over half of women exceed the IOM recommendations for weight gain during pregnancy (Weisman, Hillemeier, Symons Downs, Chuang, & Dyer, 2010), which has been an increasing trend over the last 25 years. Obese pregnant women are at increased risk of preeclampsia, gestational diabetes, cesarean section, and induced labor and are more likely to have large for gestational age or macrosomic neonates (Athukorala, Rumbold, Willson, & Crowther, 2010). Additionally, the prevalence of smoking during pregnancy is currently 10 to

20%, and this trend has not changed since the late 1990s (Ebrahim et al., 2000; Swamy et al., 2011; Tong et al., 2013).

Findings from qualitative studies have found that women's inability to quit smoking during pregnancy is often a source of more guilt and perceived stress, perpetuating a behavioral-emotional feedback cycle that makes the behavior even more difficult to change (Murray, Small, & Burrage, 2014). High stress levels have been associated with lower tobacco abstinence rates, and evidence suggests that women face different barriers and stressors than men related to quitting, such as higher rates of depression and greater weight-related concerns (Centers for Disease Control and Prevention [CDC], 2012). Smoking during pregnancy is associated with numerous adverse effects including multiple-organ birth defects (Hackshaw, Rodeck, & Boniface, 2011) and restricted fetal organ growth (Anblagan et al., 2013).

Furthermore, 7.6% of pregnant women report alcohol use during the prior 30 days, and 1.4% report binge drinking (CDC, 2012), although these self-report estimates are likely to be underestimates. Additionally, nearly a quarter (22%) of pregnant women do not take a folic acid supplement (Branum, Singer, & Bailey, 2012).

Health behavior interventions based on patient education alone, such as individual counseling and distribution of health information, have demonstrated limited effects (Filion et al., 2011; Guelinckx, Devlieger, Mullie, & Vansant, 2010; Kinnunen et al., 2007). A recent meta-analysis of randomized-controlled intervention studies (N = 44 studies) examined the effect of weight control interventions during pregnancy (Thangaratinam et al., 2012). Overall, the analysis found that participants in weight control interventions gained a modest 1.4 kilograms less than control participants, and no differences were found in meeting IOM pregnancy weight gain recommendations (Thangaratinam et al., 2012). Another meta-analysis (N = 8) of

randomized controlled studies examining smoking cessation counseling during pregnancy did not find evidence to suggest that these interventions were effective in promoting abstinence (Filion et al., 2011). Alternatively, addressing women's strategies for coping with stress, rather than lack of knowledge, may be a better target for improving engagement in positive health behaviors (Wright et al., 2013).

While many studies have established evidence of the adverse effects of stress (Wadhwa, Entringer, Buss, & Lu, 2011), poor health behaviors (Alhusen, Gross, Hayat, & Sharps, 2012) and cortisol (Buss et al., 2009) on birth outcomes, few studies exist to establish evidence of the specific relationship of cortisol regulation during pregnancy with the various dimensions of lifetime stress. Additionally, it is unknown whether coping attenuates the effects of stress on cortisol regulation, health behaviors and birth outcomes (see Figure 1).

Figure 1 presents a model of the proposed study based on these theoretical perspectives, displaying established and hypothesized relationships among the key concepts within the context of the study aims and analytic approach.

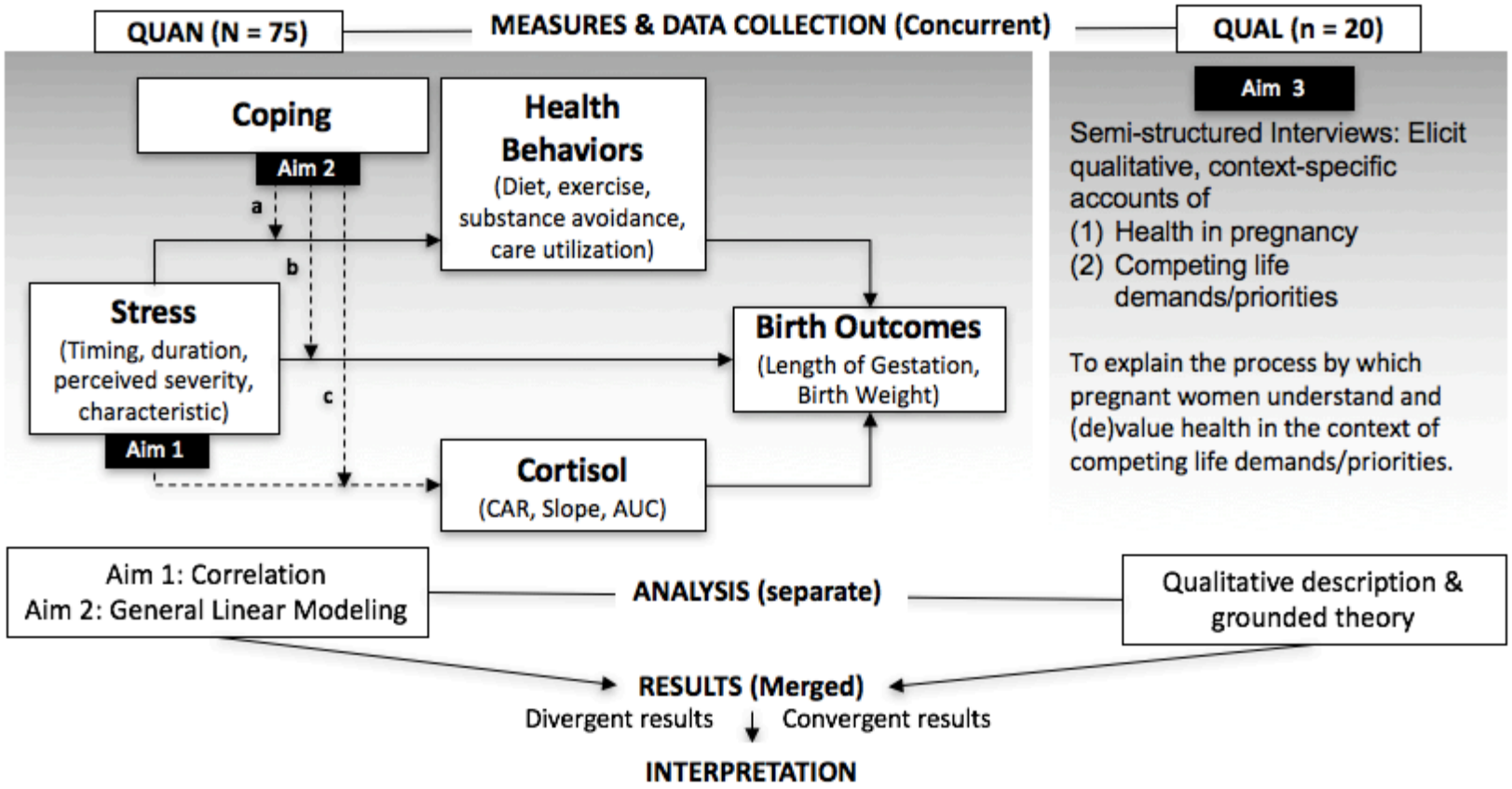

Figure 1. Conceptual model.
The quantitative arm will examine the relationships between stress, coping, cortisol, health behaviors and birth outcomes. Analyses will examine correlational relationships between stress and cortisol (Aim 1), followed by general linear modeling (Aim 2) to determine whether coping styles moderate the influence of a) stress on health behaviors, b) stress on birth outcomes, and c) stress on cortisol. Solid lines represent established relationships, while dashed lines represent the relationships that are being tested in this study. A qualitative arm (Aim 3) will use semi-structured interviews and qualitative description of women's experiences of stress and coping. The two arms will be collected concurrently and analyzed separately. The results from each arm will be merged by describing convergent and divergent findings, followed by an interpretation of the combined results.

MANUSCRIPT 1

AN INTEGRATIVE REVIEW OF THE INTERGENERATIONAL TRANSMISSION OF MATERNAL EARLY LIFE ADVERSITY VIA HPA AXIS DYSREGULATION DURING PREGNANCY

Abstract

Objective: To review published literature on the intergenerational transmission of maternal early life adversity (ELA) via hypothalamic-pituitary-adrenal (HPA) axis dysregulation during pregnancy. Data Sources: A comprehensive literature search of PubMed, CINAHL, and PsychINFO databases using variants of the keywords childhood, violence, abuse, trauma, pregnancy, HPA and cortisol. Study Selection: Titles and abstracts were reviewed, and full-text articles retrieved and analyzed that met the inclusion criteria: 1) pregnant or recently delivered, 2) included a measure of HPA axis pathway (cortisol, ACTH, CRH) or genetic / enzymatic regulators of the HPA axis, 3) measure of maternal early life adversity and 4) published in English in a peer-reviewed databased journal with unrestricted publication date. Data Extraction: Extracted data included study author, design, sample size, methods and measures, and major findings with regard to maternal biomarkers and newborn outcomes. Data Synthesis: An integrative review was conducted as described by Whittemore and Knafl (2005). Results: Eleven articles were included in the review, examining either cortisol or corticotrophin releasing hormone. No articles were found using other HPA biomarkers. Conclusion: There is a small, but growing body of literature on the long-lasting effects of early life adversity on HPA axis regulation in pregnant women. Although changes in the HPA axis are also evident in non-pregnant samples, there are specific changes that occur in the HPA axis during pregnancy.

Keywords: HPA, cortisol, CRH, childhood adversity, prenatal

Early life adversity (ELA) is associated with health and disease trajectories over the lifespan (Seckl & Holmes, 2007). ELA can be especially damaging because it occurs during critical periods of childhood development during which adverse experiences are linked with epigenetic changes involved in regulating the hypothalamic-pituitary-adrenal axis (HPA) (Anacker, O'Donnell, & Meaney, 2014; Parrott et al., 2014; Turecki & Meaney, 2016). Periods such as fetal development and early childhood are times most susceptible to adverse experiences such as childhood maltreatment, abuse, neglect and exposure to violence. ELA negatively impacts children's capacity for learning, regulating behavior, and later health outcomes (Shonkoff & Garner, 2012). The relationship between ELA and adult health outcomes is strong and graded, such that greater exposure to adversity leads to greater health risks later in life (Felitti et al., 1998). Individuals with six or more adverse childhood experiences die on average 20 years earlier than those who do not experience any childhood exposures. Furthermore, the CDC (2016) estimates that the lifetime cost of child maltreatment is 124 billion dollars due to lost productivity, health care costs, special education, child welfare, and criminal justice.

There is also evidence that the effects of early adversity experienced by parents may be passed on intergenerationally to their offspring via psychological, biological, biophysical, and behavioral mechanisms (Buss et al., 2017). The effects of ELA on women is of particular concern due to potential alterations that may manifest during pregnancy within the gestational environment (Seckl & Holmes, 2007). In addition, women typically have much influence over the postnatal environment as primary caregivers. Childhood maltreatment is associated with numerous health risks for women, including substance abuse, depression, suicide attempt, smoking, sexually transmitted disease, obesity, financial stress, poor academic achievement, unintended pregnancy, adolescent pregnancy and in-utero fetal death (CDC, 2016), all of which can impede pregnancy health and adequate parenting. Pregnant mothers with prior history of

trauma have infants with lower birth weight, greater negative affect, and shorter gestations (Smith, Gotman, & Yonkers, 2016). Research shows that severe sexual and physical abuse in childhood is associated with up to a 2-fold increased risk for preterm birth (Christiaens, Hegadoren, & Olson, 2015). The complexity of the biological processes linking ELA and adverse birth outcomes are now beginning to emerge (Kalmakis, Meyer, Chiodo, & Leung, 2015; Nusslock & Miller, 2016).

Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis is one of the most studied biological links between ELA and lasting health outcomes (Tarullo & Gunnar, 2006). In women, ELA is linked to HPA dysregulation. Women with ELA have greater cortisol reactivity to stress, higher incidence of depression and post-traumatic stress symptoms, lower psychological resilience, excessive alcohol use, insecure attachment, re-victimization, and altered self-schemas (Gallo et al., 2017; Hannan, Orcutt, Miron, & Thompson, 2017; Kaye-Tzadok & Davidson-Arad, 2017; Lee & Chen, 2017; Mielock, Morris, & Rao, 2017; Stanton, Meston, & Boyd, 2017; Till-Tentschert, 2017; Zietlow et al., 2017).

Nurses have long recognized the importance of addressing psychosocial issues in prenatal care, especially issues such as intimate partner violence, abuse and depression during pregnancy (Cole, Scoville, & Flynn, 1996; Sperlich et al., 2017; Tilden, 1983). Rarely do these issues arise spontaneously, but rather are rooted in cyclical patterns across generations. Therefore, it is important to address the specific abuse-related issues that arise for women during pregnancy, as well as anticipate the problems that may occur after delivery.

Definitions

Child maltreatment is one of the most damaging and chronic forms of early life adversity, and is defined as an act of commission (i.e. physical, sexual, or emotional abuse) or omission (i.e. physical or emotional neglect) by a parent or other caregiver resulting in actual harm, potential for harm, or threat of harm to a child (CDC, 2016). In the United States, 13% of girls experience substantiated maltreatment before 18 years of age, which is likely an underestimate representing particularly severe or persistent cases (Wildeman et al., 2014). In adulthood, these women are at risk for experiencing lifelong emotional, relational and physiologic effects as a result, including depression, intimate partner violence and physiologic dysregulation across body systems (Kendler & Aggen, 2014; Lee, Coe, & Ryff, 2017; Mccloskey, 2016), with specific effects on women's pregnancy health and outcomes (Cammack et al., 2011; Records & Rice, 2009; Smith et al., 2016; Winn et al., 2003).

The intergenerational transmission of ELA refers to the negative relational and physiologic effects that are transmitted to offspring of parents who have been maltreated or experience other severe adversity as children (Buss et al., 2017; Widom & Wilson, 2015). While the relational aspects of intergenerational transmission have been a topic of interest among psychologists for several decades (e.g. cycles of abuse and re-enactment of relational patterns within families) (Bartlett, Kotake, Fauth, & Easterbrooks, 2017; Cicchetti & Rizley, 1981; Main & Goldwyn, 1984; Zeanah & Zeanah, 1989), more recent focus has been on the additional biological effects of maternal childhood maltreatment transmitted to offspring via the gestational environment during pregnancy (Buss et al., 2017).

The HPA axis plays a major role in the human response to stress. The primary stress response pathway within the HPA axis begins when a stressful situation triggers the release of

corticotrophin-releasing hormone (CRH) from the paraventricular nucleus of hypothalamus to the anterior pituitary. The pituitary then responds by releasing ACTH and β endorphin. ACTH circulates systemically where it cues the adrenal glands to release cortisol. Cortisol then disperses and binds to glucocorticoid receptors in tissues throughout the body to mobilize energy stores and prepare to fight or flee. Cortisol exerts negative feedback on the hypothalamus and pituitary to decrease further stimulation of cortisol secretion. Dysregulation of the HPA axis has been linked with a wide variety of physical and mental health outcomes, including depression, obesity, cardiac and immune diseases (Lupien, McEwen, Gunnar, & Heim, 2009; Nicolaides, Charmandari, Chrousos, & Kino, 2014).

HPA Axis in Pregnancy

Changes occur within the HPA axis in women during pregnancy, most notably the growth of the placenta (of fetal origin) as a transient endocrine gland and nutrient transporter (Wadhwa, Dunkel-Schetter, Chicz-DeMet, Porto, & Sandman, 1996). As a result, cortisol levels increase two to four-fold over the course of gestation. Part of this increase is due to placental CRH production in response to rising cortisol levels, resulting in a positive feedback loop between maternal cortisol and placental CRH. Because of the increases in cortisol over the course of pregnancy, down-regulation of maternal hypothalamic CRH occurs, and the overall maternal stress response is dampened. Maternal response to elicited stressors is attenuated as gestation advances, including both perceived psychological stress and sympatho-adrenal medullary response (i.e. heart rate and blood pressure) (Entringer et al., 2010). Cortisol awakening response attenuates towards the end of pregnancy, normally showing a smaller peak at 30 minutes after awakening during late pregnancy compared to early pregnancy (Entringer et al.,

2010). The dampened maternal stress response in late pregnancy may serve as a protective mechanism against severe stressors in late gestation (Entringer et al., 2010).

Maternal cortisol partially crosses the placenta and is involved in fetal brain growth, organ development and timing of delivery (Buss et al., 2009). As such, cortisol helps to ensure that delivery occurs when the fetus's organs are mature and developed enough to survive as a newborn (Mesiano, 2016). Therefore, alterations in the mother's HPA axis functioning during pregnancy, and transport of cortisol across the placenta has ramifications for development of the fetus. It is for this reason that the long-term maternal HPA alterations related to childhood maltreatment are significant for pregnancy and fetal programming.

Dysregulation in the maternal HPA axis during pregnancy is implicated in numerous short- and long-term health consequences in infants, including negative infant affect, poor emotional regulation, and altered cardiac vagal control (Bolten et al., 2013a; Bosquet Enlow et al., 2017; Rash, Campbell, Letourneau, & Giesbrecht, 2015). Dysregulation of maternal cortisol during pregnancy has also been linked with structural brain deficits in infants, impaired cognitive performance in children (Davis, Head, Buss, & Sandman, 2017) and child psychopathology (Isaksson, Lindblad, Valladares, & Högberg, 2015). Structural brain alterations are also evident in newborns prior to exposure to the postnatal caregiving context (Buss et al., 2016). In contrast, other studies have found that higher maternal cortisol levels in the third trimester have been associated with greater cortical thickness and enhanced cognitive performance in children (Davis et al., 2017). Together these findings suggest that the altered functioning of a woman's HPA axis is linked with altered brain development in the fetus that persist into childhood.

Purpose

While many of the biological HPA mechanisms underlying the association between ELA and health effects in adults have been previously reviewed (Shea, Walsh, MacMillan, & Steiner, 2005), we are not aware of any reviews that have integrated findings specific to pregnancy biomarkers of HPA axis functioning as they relate to ELA history. The purpose of this article is to review the body of literature linking women's experience of ELA with later HPA dysregulation during pregnancy. We will provide a definition for HPA dysfunction as a concept based on the evidence available, as well as review the theories and methods that are currently being used to support this line of research. Since ELA is closely associated with depression and adversity in adulthood, we also examined how depression factors into the results. Finally, we will discuss the relevance of these findings to evidence-based nursing practice and research in regard to pregnant women who have experienced ELA, with an emphasis on the psychosocial aspects of care.

Methods

An integrative review was conducted as described by Whittemore and Knafl (2005). This approach includes stages of problem identification, literature search, data evaluation, and data analysis. This review approach was selected for its capacity to accommodate a variety of methodological approaches, types of data, and a wider range of purpose. This review approach allows for "a comprehensive portrayal of complex concepts, theories, or health care problems of importance to nursing" (p.548).

A literature search of PubMed, CINAHL, and PsychINFO databases using combinations of the keywords childhood, violence, abuse, trauma, pregnancy, HPA and cortisol. Articles were considered for inclusion if they included a sample of pregnant women and measured HPA

biomarker(s) (e.g. cortisol, ACTH, CRH, or other HPA-related biomarkers) and assessed maternal history of ELA. Articles also needed to be published in English in a peer-reviewed, databased journal article. Articles were not limited by year of publication. Data were extracted from articles and placed into a table including author, study design, sample description, methods and measures, and major findings with regard to maternal biomarkers and birth outcomes (Table 1).

Results

A total of eleven articles were identified for inclusion in the review, listed in Table 1. Three articles reported on the same study (Bublitz et al., 2014; Bublitz & Stroud, 2012, 2013). All but one study examined cortisol as a biomarker of HPA functioning. The exception examined CRH. Sampling methods for cortisol collection included saliva, plasma and hair, while CRH was measured in plasma.

A majority of the studies were conducted with samples of mostly low-income minority women living in the United States, with the exception of one study conducted in Canada, and one study conducted in Germany. The mean age of participants in non-US studies tended to be older (32 years) than participants in the US-based studies (26 years). All studies were prospective and included observational (n = 5) or longitudinal designs (n = 5) (see Table 1). One study utilized a matched case-control design comparing women with term and preterm deliveries. Samples sizes ranged from small pilot studies (N = 17) to larger studies (N = 295). All were conducted with pregnant women 20 weeks gestation or later, except two studies which collected data across gestation, including the first trimester (Moog et al., 2016; Walsh et al., 2016).

Early Life Adversity Measures

Early life adversity was measured using either the Adverse Childhood Experiences Survey (ACES) (Dube et al., 2003), Childhood Trauma Questionnaire (CTQ) (Bernstein & Fink, 1998), or the Stress and Adversity Inventory (STRAIN) (Slavich & Epel, 2010). Ten of the items in the ACES were derived from the CTQ, and therefore the scales are very comparable. The STRAIN is a broader measure assessing stress over the life course, and includes items related to childhood abuse and neglect as well as items related to other types of childhood adversity (e.g. bullying, death of a loved one). All of these tools have been shown to have good reliability and validity. The CTQ has good internal reliability (Cronbach α = .79 - .94) and test-retest reliability (intraclass correlation = 0.88 over 2 – 6 month interval), as well as convergent validity with interview-based measures (Bernstein et al., 1994). The ACES has demonstrated validity by repeatedly showing a strong graded relationship to a variety of health problems (Dube et al., 2003) as well as moderate to substantial test-retest reliability (Kappa = .64, <11% discordance over time) (Dube, Williamson, Thompson, Felitti, & Anda, 2004).

Scoring of adversity measures. The CTQ is 28 items with five subscales: physical, emotional, and sexual abuse and physical and emotional neglect. The CTQ uses a 5-point frequency of occurrence scale ranging from 1 (never true) to 5 (very often true). The ACES also includes items on physical, emotional and sexual abuse and physical and emotional neglect, as well as household dysfunction. Most response options ranging from 1 (never) to 5 (very often). For both scales, scores in each category are summed. Early studies using the ACES summed the number of categories of abuse that were experienced (rather than total scores across all items), and demonstrated a graded association such that the more categories of abuse were associated with worse health outcomes (Felitti et al., 1998). Only two studies included in this review analyzed the childhood maltreatment scores as categories of abuse (Bublitz et al., 2014; Moog et al.,

2016). The remaining studies analyzed maltreatment data as either continuous variables or split into categorical groups of two or three based on type of trauma exposure. Among the studies using a categorical approach, two studies analyzed sexual and physical abuse together as a separate category from other types of abuse (Bublitz, Bourjeily, Vergara-Lopez, & Stroud, 2016; Schreier et al., 2016), while another two articles analyzed sexual abuse separately from non-sexual abuse (Bublitz & Stroud, 2012b, 2013). The remaining five articles analyzed childhood maltreatment as a total score on a continuous scale. Overall, three main approaches to analyzing abuse were used: summed categories of abuse, continuous scores, or dichotomous groups.

Biomarker Collection and Analysis

Two key hormones within the HPA axis were examined within the reviewed studies: CRH and cortisol. Only one study (Moog et al., 2016) examined CRH in relation to ELA. The 10 remaining studies used cortisol as a biomarker, measured in either saliva, hair or plasma. Cortisol is described by three types of parameters: cortisol response, cortisol recovery or total daily cortisol production. Dysregulated HPA systems are characterized by blunted, excessive, or prolonged responses (McEwen, 1998). The response and recovery estimates are typically measured using saliva collection over time. The natural diurnal rhythm is measured as a response-recovery dynamic, characterized by a cortisol awakening response (CAR) typically occurring 30 to 45 minutes after awakening (Sandman et al., 2006). The CAR is followed by a gradual decrease, or diurnal slope, over the course of the day with cortisol levels dropping much lower than morning baseline level.

An estimated 80% to 90% of maternal cortisol is metabolized by the placental enzyme 11 beta-hydroxysteroid dehydrogenase type 2 (11β-HSD) (Gitau, Cameron, Fisk, & Glover, 1998). Despite this high level of metabolism, the maternal-fetal cortisol ratio is 11:4, with maternal

cortisol levels accounting for 40% of the variance of fetal levels (Gitau et al., 1998). Several recent studies have examined how various maternal factors down-regulate, or decrease the efficiency by which 11β-HSD oxidates cortisol. These factors include maternal depression and anxiety, infection, and substance abuse. Maternal stress also influences epigenetic alterations in the expression of the 11β-HSD enzyme, resulting in greater levels of maternal cortisol transferred through the placenta to the developing fetus (Marsit, Maccani, Padbury, & Lester, 2012).

Corticotrophin Releasing Hormone

Moog et al. (2016) measured plasma CRH longitudinally in pregnancy over five time points between 15 and 37 weeks gestation. Since plasma CRH during pregnancy is almost entirely produced by the placenta, plasma CRH is considered to be of placental origin. The study found that childhood trauma was associated with a 25% increase in placental CRH towards the end of pregnancy. Higher CRH has been associated with preterm birth in prior studies (Wadhwa et al., 2004).

Cortisol

Prior studies using cortisol as a measure of HPA dysfunction in non-pregnant samples have used estimates of cortisol response to stressors in both naturalistic and laboratory settings. The method of ecological momentary assessment was used by one study (Bublitz et al., 2016) to assess women's cortisol response to naturally occurring daily stressors. In this method, women were sent texts at semi-random intervals throughout the day, and asked to rate their momentary level of stress. Thirty minutes following the initial text, another text was sent asking them to collect saliva in order to estimate the cortisol response to the momentary rating of stress. The study found that women who have been maltreated as children have blunted cortisol response to momentary stress compared to non-abused women.

Another naturalistic measure of cortisol response is the morning response that occurs in relation to prior day stress, or the evening recovery that occurs in relation to same-day stress. Bublitz and Stroud (2013) found that women who have experienced childhood sexual abuse had greater morning cortisol in relation to prior day stress and greater evening cortisol in relation with same-day stress, both suggesting a prolonged cortisol response.

In pregnant women, a unique aspect of cortisol regulation is that the CAR attenuates, so that the size of the increase from awakening to 30 minutes after awakening gradually decreases towards the end of gestation (Entringer et al., 2010). Bublitz and Stroud (2012) found that women who had experienced childhood sexual abuse did not have the normal attenuation of CAR, but rather an increasing CAR in late gestation (35 weeks) compared to non-abused women. Not only this, but they found that sexual abuse was particularly unique in that the CAR also increased in comparison to women who experienced non-sexual abuse as a child, suggesting that childhood sexual abuse, specifically, leads to long term dysregulation of the HPA axis that persists into pregnancy. While the size of the morning response is larger, other researchers have found that initial baseline morning levels are lower with increasing severity of abuse (Shea et al., 2007).

Another estimate is total cortisol, measured either by calculating area under the curve based on multiple salivary sampling points throughout one or more days or through hair cortisol analyses. One study using saliva found that total daily cortisol as measured by area under the curve (AUC) was not associated with abuse history in pregnant adolescents, although cortisol AUC did mediate the relationship between IL-6 and shorter gestation (Walsh et al., 2016), suggesting an interplay between the immune and HPA systems.

Plasma Cortisol. A recent study examining a single sample of plasma cortisol in African American pregnant women at 30 weeks gestation found that childhood stress was associated with higher cortisol levels, and further, that cortisol levels mediated the relationship between certain subtypes of stress (interpersonal loss and physical danger) and the timing of birth. Among women who delivered spontaneously, the timing of birth occurred 7.5 days earlier if they had experienced levels of childhood stress reaching two standard deviations above the mean. This study was particularly well designed in that it controlled for levels of adulthood stress. In contrast to childhood stress, adulthood stress was not associated with the timing of birth. Nor did adulthood stress affect the relationship between childhood stress and timing of birth. This finding is in contrast to a number of other studies suggesting that stress during pregnancy is associated with the length of gestation (Bussières et al., 2015). These findings highlight the salience of trauma occurring during sensitive childhood periods of development as compared to adulthood. Few studies examining stress during pregnancy have taken into account childhood stress.

Hair Cortisol. Three studies analyzed hair cortisol in relation to childhood trauma. Hair can be collected shortly after delivery, and then analyzed for each trimester of pregnancy, assuming each centimeter of hair represented one month of hair growth. Nine centimeters of hair collected shortly after birth provides an estimate of total cortisol over the entire pregnancy (Schreier, Enlow, Ritz, Gennings, & Wright, 2015).

In one study, hair cortisol in women were compared between those delivering term and preterm in a matched case-control study. This study found that women who delivered preterm had lower hair cortisol compared to control women matched for length of gestation, which was somewhat unexpected given that preterm birth has usually been associated with higher cortisol levels (Giurgescu, 2009). The difference in these findings could be due to the different forms of

cortisol estimates that hair and saliva provide. While hair estimates total cortisol over the entire pregnancy, salivary cortisol only provides an estimate at one defined time point within a constantly changing circadian rhythm. The study did find that childhood emotional neglect was associated with preterm delivery (Karakash et al., 2016).

In another larger study examining hair cortisol over all trimesters, sexual and physical abuse were associated with higher hair cortisol, but only for African American or black pregnant women, and not white or Hispanic women (Schreier et al., 2015). This is the only reviewed study that analyzed racial differences, and is an area for further investigation, particularly considering high rates of preterm birth and infant mortality among black women.

Finally, Schury et al. (2017) analyzed hair cortisol in the 3rd trimester among an older, well-educated sample of German pregnant women and their infants. This study found that childhood maltreatment was associated with elevated dehydroepiandrosterone (DHEA) in hair, but not cortisol for both mothers and infants (Schury et al., 2017). This is in agreement with the study by Schreier et al. (2015) in that child maltreatment is not associated with elevated hair cortisol in Caucasian pregnant women. These findings are in contrast to prior studies in non-pregnant samples linking adverse childhood experiences with lower levels of hair cortisol (Kalmakis et al., 2015).

Depression and Adulthood Adversity

In this review, we also examined whether studies included depression as a covariate, and how this related to both biological and trauma-related measures. The majority of studies (n = 7) reported measuring depression. Two studies reported no difference in levels of depression or daily stress between abused and non-abused groups (Bublitz et al., 2016; Bublitz & Stroud, 2012b, 2013), while another study with a younger, adolescent sample did find significant

medium-sized correlations between child abuse and depression in pregnancy (Walsh et al., 2016). Bublitz, Parade, and Stroud (2014; 2013) reported depression levels in relation to cortisol, and found that depression did not predict cortisol levels or CAR over time, while childhood sexual abuse did predict increasing CAR over the duration of pregnancy. Similarly, Shea et al. found that childhood trauma explained 12% of the variance of awakening cortisol, while symptoms of anxiety and depression during the current pregnancy were not associated with cortisol. Walsh et al. (2016) also found that cortisol AUC during second and third trimesters was neither associated with depression nor childhood trauma.

Bublitz and Stroud (2013) found that childhood sexual abuse moderated the association between self-reported stress levels and evening cortisol levels, such that sexually abused women had higher cortisol levels in the evening as daily stress increased. This study also found that prior day stress was associated with cortisol at 30 minutes after awaking the next day. As prior day stress increased, abused women had higher cortisol levels in the morning. These authors suggest that altered cortisol response to stress during pregnancy may link childhood abuse (especially sexual abuse) and adverse neonatal outcomes (Bublitz & Stroud, 2013).

Only one study measured both childhood and adulthood stress. This study found that only childhood stress was associated with cortisol and birth timing (Gillespie, Christian, Alston, & Salsberry, 2017), in contrast to the findings of many previous studies demonstrating associations between perinatal stress and pregnancy outcomes (Bussières et al., 2015).

Protective Factors

The findings of two other studies suggest that adulthood factors could moderate the effect of childhood experiences on pregnancy outcomes. In one study looking at childhood sexual abuse, the authors found that better family functioning during pregnancy moderated the

association between abuse and the CAR. Abused women with better family functioning had CAR trajectories across pregnancy that looked more similar to non-abused counterparts, suggesting that current family functioning could have a protective or reparative effect on HPA dysfunction during pregnancy (Bublitz et al., 2014). A similar finding was discovered by Walsh et al. (2016) in that pregnant adolescents who experienced high levels of abuse, but low levels of depression during pregnancy had lower levels of inflammation (i.e. IL-6) compared to abused counterparts with high levels of depression. These findings point to the possibility that better family functioning and healthy mood during pregnancy could mitigate the dysregulating effects of childhood abuse on HPA functioning in adulthood.

Relation to Immune System

Only one study reported the results of cortisol in relation to immune factors during pregnancy (Walsh et al., 2016). The study included a sample of mostly Latina adolescents. Cortisol was significantly associated with levels of IL-6 during the second trimester ($r = 0.21$, $p<0.05$). Abuse and depression did not predict levels of immune factors (i.e. IL-6 and CRP) in pregnancy. Although, an interaction effect was found between depression and childhood abuse such that adolescents who were severely abused as children and were more depressed during pregnancy had higher IL-6 levels during the second trimester of pregnancy. In turn, higher IL-6 was associated with shorter gestation, which was moderated by cortisol. These findings add to evidence that immune and HPA systems interact to predict pregnancy outcomes.

Neonatal Outcomes

There were mixed results among the studies that reported on neonatal birth outcomes. Several studies did not find an association between childhood abuse and birth outcomes such as gestational age at delivery, birth weight or Apgar scores (Bublitz et al., 2016, 2014; Bublitz & Stroud, 2013). However, other studies did find positive associations. Gillespie et al. (2017b)

found that higher levels of childhood stress predicted shorter gestation and that this relationship was mediated by plasma cortisol levels. Furthermore, Karakash et al. (2016) found that higher childhood emotional neglect was associated with preterm birth. The remaining articles did not report on birth outcomes (Bublitz & Stroud, 2012b; Moog et al., 2016; Schreier et al., 2016; Shea et al., 2007).

Discussion

Overall, the findings from these studies provide preliminary evidence that women who have been exposed to ELA as children display altered HPA function during pregnancy, some of which are specific to pregnancy (i.e. lack of attenuation of CAR and increases in CRH towards late gestation), although not all studies found significant relationships between ELA and cortisol. Collectively these studies suggest a pattern of dysregulation in which the diurnal pattern of cortisol over the trajectory of pregnancy does not follow typical patterns of CAR attenuation, while at the same showing a blunted response to acute, momentary stressors, and lower baseline morning levels. This small but growing body of literature on the long-lasting effects of ELA on HPA axis regulation demonstrates that there are several pregnancy specific changes that occur during pregnancy including markedly increased levels of CRH, ACTH, and cortisol in pregnancy, as well as a down-regulation of the capacity for the maternal HPA axis to respond to stressors. In women who have experienced ELA in the form of childhood maltreatment, particularly sexual abuse, HPA regulation is altered in several distinct ways that suggest a dynamic and complex relationship between abuse and HPA regulation, including dampened, heighted or prolonged responses to stress.

Only a few of the reviewed studies found significant results in regard to depression. This could be due to a couple reasons. First, most of the studies included samples of women from

lower socioeconomic populations. The baseline levels of depression could be higher in these women related to current challenges and living situations, regardless of their experience of childhood adversity. High levels of depression across the sample may have masked the association between early childhood adversity and depression. Also, the null findings could have been due to the use of depression as a continuous variable in the analyses, rather than dichotomous. Prior studies have shown that dichotomous analysis of depression results in larger, more significant effect sizes (Grote et al., 2010).

Variable methods of HPA biomarkers were used across studies. Although standardized measures are typically desired, in the case of HPA there are several aspects of regulation that make up a broader picture of HPA function. Thus, the variety of cortisol measures serves to enhance the findings by providing multiple points of abuse-related alteration. Across studies that measured salivary cortisol, all of the studies collected multiple saliva samples across multiple days, which is a strength that serves to reduce the limitation of variability that occurs in cortisol over the course of a day, and between days.

The integrated findings presented here are in line with other studies of mothers who have been abused or experienced trauma during childhood. These women are more likely to have infants with a more negative affect (Bosquet Enlow et al., 2017) but also more likely to have more attuned cortisol patterns (i.e. synchrony) with their children's cortisol patterns as toddlers (Fuchs, Moehler, Resch, & Kaess, 2017). The offspring of abused mothers also have significantly higher internalizing symptoms, such as anxious and depressed behaviors during childhood. This relationship remained present even after controlling for maternal harsh parenting practices and maternal depression, suggesting that intergenerational transmission occurs through pathways outside of postnatal psychosocial risks such as maternal mood or parenting practices (Esteves, Gray, Theall, & Drury, 2017). As adolescents, these children are at greater risk for smoking,

overweight and obesity (Roberts et al., 2014). In pregnant women, ELA is also associated with infection, even after controlling for current stress and adversity (Cammack et al., 2011), suggesting perhaps a superseding effect of early adversity over adult adversity.

Several interdisciplinary lines of theory converge to underlie the scope of this review. The first is the notion of biological embedding, with regard to both maternal ELA and the HPA impacts on the fetus. The biological embedding of maternal childhood maltreatment is further explained by the theories of allostasis and allostatic load (McEwen, 1998). Allostasis is the resetting of physiologic set-points as an adaptive response to recurrent or chronic stress exposure, such as childhood maltreatment and the associated dysfunctional family dynamics. While allostatic adjustments may be adaptive in the short-term, overload of physiologic systems may eventually predispose individuals to chronic disease and poor health (McEwen, 1998). This overload has been referred to as allostatic load. Allostatic load is the wear and tear on the body that occurs as a result of chronic exposure to stress. Within the literature of child development, the stress preceding allostatic load is referred to as toxic stress (Shonkoff et al., 2012). Over time, toxic stress leads to allostatic load across multiple, interdependent physiologic systems, central of which is the HPA axis.

The biological embedding of maternal ELA leads to allostatic load reflected in the HPA axis. The HPA axis is an important source of information transmitted via the placenta to the fetus. From an evolutionary perspective, this hormonal information from the mother encourages certain trajectories of neural, hormonal, and organ system growth. During this critical period of development, movement towards certain trajectories over others is thought to be relatively stable. In the case of dysregulated maternal HPA axis, the programming of fetal development is perturbed within the altered gestational environment (Reynolds, Labad, Buss, Ghaemmaghami, & Raikkonen, 2013; Seckl & Holmes, 2007). Ostensibly, this results in long-term alterations in the

potential for certain health and disease trajectories over the lifespan (Godfrey & Barker, 2001). Early programming ideally would serve in the interest of fetal survival in extra-uterine life. However, these early junctures in the fetus's developmental trajectory may not align with the actual environment encountered. In this case, the prenatal period becomes an early origin of childhood and adult disease and psychopathology (Buss et al., 2012; Gluckman & Hanson, 2006).

In many cases there is a mismatch between the types of stress the fetus is prepared for versus what types of stress are actually encountered. Fetus's who are primed during the prenatal period to have a highly functioning and very reactive HPA system are born into a world in which composure, emotional stability and mental focus are the traits needed for success. Generally speaking, a hyper-reactive HPA axis will not foster such needed qualities in offspring, but rather will predispose children to higher rates of externalizing disorders such as ADHD. The underlying assumption is that having a relatively normal stress response is a prerequisite for normal human behavior and response to stress (Pereira & Meijer, 2017).

Child brain development is further influenced by the relational- and attachment-related repercussions of maternal early life stress by reducing the quality of maternal caregiving and sensitivity during early childhood. The long-term relational sequelae in mothers as a result of their own ELA thereby compounds the intergenerational transmission of her experiences in the postnatal context (Finegood, Blair, Granger, Hibel, & Mills-Koonce, 2016).

Limitations

There are several limitations to the current body of literature in this area to note. The first limitation is the binary conceptualization of ELA and HPA axis. Individuals who are maltreated as children are more often than not the victims or witnesses to multiple types of violence (domestic violence, bullying, gang-related violence), often across multiple contexts (home,

school, community). Thus, maltreatment by a caregiver is co-occurring with many other types of violence and victimization, termed poly-victimization. Hamby et al. (2012) refers to the "tangled web of dysfunction" within which maltreated children live. Therefore, it is within this broader context, rather than individual abusive events, likely contribute to dysfunction in the HPA axis. While all studies measured multiple categories of maltreatment, a broader measure of violence in childhood may provide a better picture of the web of dysfunction. Some studies have found that the number of categories of abuse is more relevant than the chronicity or severity of abuse, indicative of a greater or lesser burden of victimization. Future studies could measure a broader array of victimization experiences in childhood, such as bullying, domestic violence, family dysfunction and witness to other violent events during childhood.

Also, these studies do not shed light on the mechanisms by which changes in HPA biomarkers occur, which is likely multifactorial. Maltreatment affects every aspect of life. While initial response to trauma leads to a stress response, over time, this mechanism becomes worn out. Continued wearing of the system may occur throughout adult life via abused-related changes in affect, cognition, and behavior (e.g. depression, altered self-schemas, and substance abuse).

Another limitation is the lack of inclusion of potential protective or reparative factors within the analysis. These variables would address whether certain positive or enriching environments could perhaps reverse the damage done by childhood maltreatment. There is little literature on the types of protective factors that could serve to moderate the impact of violence on women's HPA regulation after exposure to child maltreatment, such as social support and other means of enhancing resilience to trauma.

Implications for Research

As sampling and analysis methods for HPA axis biomarkers have developed over the recent years, more specific aspects of HPA regulation have been examined besides simple under- or over-activity (i.e. high or low levels of cortisol). The regulation of the HPA axis is complex, involving genes, neuropeptides, hormones, hormone receptors and target tissues. The field of research reviewed in this paper demonstrates this point well. While child maltreatment was shown to increase cortisol in some instances (e.g. CAR over pregnancy, in response to prior day stress, and evening levels in response to daily stress), it was associated with decreased cortisol in other instances (e.g. decreased response to momentary stress, decreased morning baseline cortisol). Genetic factors surely play a moderating role in hormone production and hormone receptors, as do protective factors such as supportive family environments (Bublitz et al., 2014). Although it would be difficult to account for all of these factors in a single study, future studies could begin to integrate more of these variables, including genetics, inflammatory factors, HPA axis mechanisms, psychosocial factors, and family and community factors.

Although the findings presented here provide preliminary support for a relationship between HPA dysregulation and ELA, these findings have limited clinical applicability at this time. The use of cortisol in N of 1 studies may be a potential avenue for future research designs. In this type of design, cortisol response would not be evaluated in comparison to the mean cortisol value of a larger sample, but rather in relation to one's one biological or behavioral rhythms, such as sleep and inflammatory factors, or environmental events and contexts. A related study approach is the field of *chronomics.* This is an approach in which the rhythmicity of cortisol, rather than excessive levels of cortisol, is examined over the duration of the circadian cycle. In this type of design, the question would not be whether cortisol was too high or too low at a given point, but instead whether a response was too early or late,

prolonged, or mis-timed in relation to other aspects of the circadian rhythm (Halberg et al., 2009).

In addition to cortisol, several new avenues of biomarker research related to the HPA axis are being investigated in pregnancy, including placental gene regulation of llB-HSD2, glucocorticoid receptors, CRH and epigenetic modifications throughout the HPA system in both the mother and fetus (Cottrell, Seckl, Holmes, & Wyrwoll, 2014; Weaver et al., 2004). So far we are not aware of any studies that have made specific links between these biomarkers as it relates to women's history of childhood maltreatment and pregnancy.

The analysis of cortisol in hair is a relevant new method for examining cortisol in pregnancy, allowing researchers to estimate the overall exposure of the fetus to cortisol across the entire pregnancy. Recent developments in the analysis of cortisol in hair have shown that hair cortisol concentrations are accurate measures of long-term free cortisol concentrations, and correlate most closely with measures of average salivary cortisol area under the curve (Short et al., 2016). Hair samples have also been used to estimate 11β-HSD activity by examining the relative amount of cortisol to cortisone in hair. 11β-HSD activity has previously been examined within the placenta, but not using hair in pregnant women. This may be an avenue for future research.

Recent studies of pregnant women exposed to war trauma have examined placental and cord blood expression of genes coding for brain-derived neurotrophic factor (BDNF), which is involved in brain growth and plasticity (Kertes et al., 2017). Another recent study found socioeconomic disadvantage to be related to transcriptional profiles of immune activation and slower tissue maturation in the placenta and cord blood (Miller et al., 2017). Others have suggested that oxytocin pathways to also be involved in the intergenerational transmission of

maternal ELA (reviewed by Toepfer et al., 2017). These are all areas for further research in relation to ELA in pregnant women.

Overall, there is a need for further investigation into the links between childhood maltreatment and maternal HPA regulation in pregnancy. The literature in this area expands prior notions of intergenerational transmission of maltreatment. Prior knowledge focused primarily on psychological and emotional mechanisms of transmission (e.g. mothering practices after birth), but these studies add further evidence of long-term biological effects that manifest in pregnancy, and the potential to program fetal brain development. This is an area of research particularly well-suited to psychiatric and obstetric nursing research because of the long-term biopsychosocial impacts on women's and children's health.

Implications for Practice

Pregnant women do not attend routine prenatal care visits expecting to be treated for their trauma. It is important, however, for providers to know how early trauma might affect the course of pregnancy, birth, and early parenting. Cole, Scoville and Flynn (1996b) identified four specific areas of concern that pregnant women frequently face during pregnancy when they have been abused as children. These concerns include depression, dissociation, maternal-infant adjustment, and sexual adjustment in couples.

Collaborative practices between nurse midwives and psychiatric nurses have been one way to address the unique mental health needs of women who have been abused (Cole et al., 1996). More recently, Sperlich et al. (2017) have described a framework in which to disrupt the intergenerational cycle of child maltreatment, with a specific focus on addressing the effects of abuse experiences on symptoms of post-traumatic stress disorder and major depression.

Furthermore, pregnancy is the initiation of intergenerational transmission of both biological and psycho-emotional experience. Impoverished women are at greater risk for having experienced trauma themselves, as well as risk for carrying the effects of that trauma forward to the next generation. Therefore, pregnancy is a timely, and potentially rare opportunity for women to have their mental health care needs addressed, especially in women who have been impacted by abuse and child maltreatment.

In addition to the biological pathways of intergenerational transmission, abuse and violent relationships within families are commonly repeated in cycles over the life course and between generations. Women who experience sexual abuse in childhood are more likely to later experience teenage dating violence, which in turn is associated with entrance into violent adult relationships (Mccloskey, 2016). In particular, women who were sexually abused as children are almost seven times more likely to enter into abusive relationships as adults (Mccloskey, 2016). Therefore, there is a strong link between experience of abuse as a child, and later experiences of abuse as an adult within intimate relationships. This is relevant within the context of pregnancy care as more and more clinics screen for intimate partner violence (IPV). IPV is not typically an isolated situation, but rather, a persistent continuation of learned helplessness and family dynamics (Renner & Slack, 2006). Therefore, addressing the effects of child maltreatment, along with IPV, can become a difficult lifelong process for women survivors of abuse.

Furthermore, it is common for women with ELA to experience depression in adulthood. Often perinatal depression research and treatment approach all women with depressive symptoms the same. However, Sperlich (2017) suggest that women who have depression and PTSD that is related to maltreatment are a subgroup of depressed women who warrant a more focused approach on interrupting cycles of abuse and vulnerability to violence.

This model is supported by studies that have found different responses to treatment based on co-morbid perinatal PTSD and depression. In these studies, women with both PTSD and depression responded to a greater extent (i.e. larger effect size) to brief interpersonal psychotherapy and/or antidepressants than did women with depression only (no PTSD or trauma). This finding suggest that more intensive levels of treatment for women with trauma-related depression are warranted (Grote, 2016). In the studies reviewed, only one found a significant association between childhood adversity and depression during pregnancy (Walsh et al., 2016). The other studies did not find that prenatal depression was associated with cortisol. In future studies it may be informative to examine prenatal depression in relation to childhood adversity, and whether cortisol differs in depressed women based on whether they have experienced ELA. This will help to inform the development of more specific and effective treatments for depression associated with ELA in women.

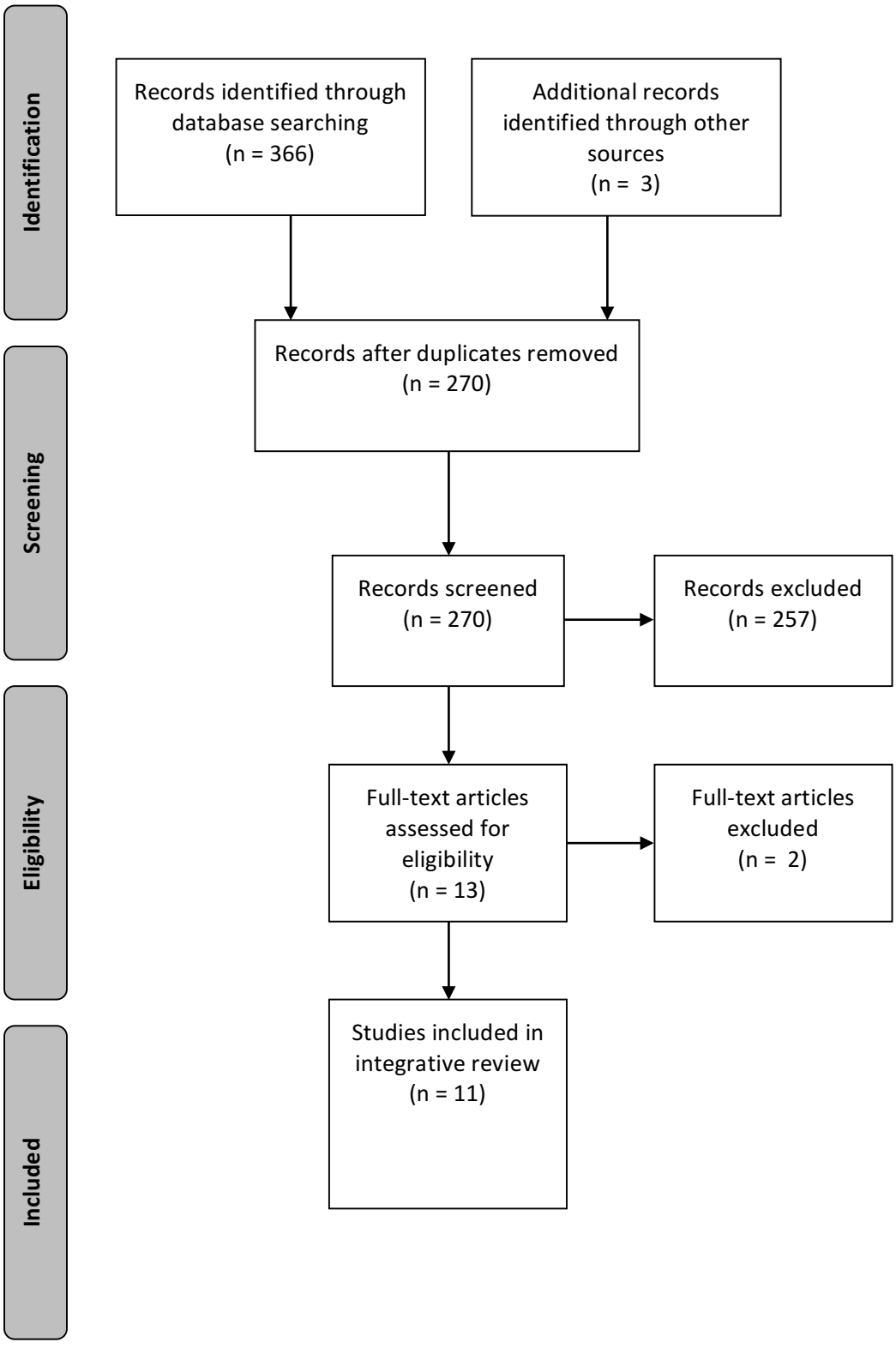

Figure 2. Flowchart of comprehensive literature review.

Table 1. Table of reviewed articles examining the relationship of ELA to HPA function in pregnancy.

Author, Year, Location	Study Design, Participants, & Sample Size	Method of Biomarker Sampling	Child Maltreatment Measures	Related Covariates	Findings	
Salivary Cortisol					**Maternal HPA Biomarker**	**Newborn Outcomes**
Bublitz et al., 2016 U.S.	Longitudinal M = 25 yrs, 47% White, 18% Hispanic, low SES N = 17	EMA Semi-random 4x/day (2 days) 27 & 34 weeks	ACES • CSA/PA: 35% • Neg/DV/NA: 65%	Momentary stress Depression Perceived Stress	Maltreatment group had attenuated cortisol response to momentary stress. Depression: No group difference	No difference in GA
Bublitz et al., 2014 U.S.	Longitudinal M = 26 yrs, 44% White, 16% Black, 29% Hispanic; low SES N = 185	CAR, slope Wake, wake + 30 min, bedtime (3 days) 25, 29 & 35 weeks	ACES Continuous	Depression Family Functioning	More severe CSA and poorer family functioning →increasing CAR Depression: no effect on CAR over time	No effect on GA, BW, or Apgar
Bublitz & Stroud, 2012 U.S.	Longitudinal M = 26 yrs, 42% White, 23% Hispanic, 14% Black, low SES N = 135	CAR, slope Wake, wake +30 min, bedtime (3 days) 24, 30 & 35 weeks	ACES • No abuse: 35% • Non-sexual abuse: 43% • Sexual abuse: 22%	Depression Anxiety Perc. Stress PTSD	Women with CSA displayed increasing CAR compared to women with no CSA (no difference in slope) Depression: no group difference	Not reported
Bublitz & Stroud, 2013 U.S.	Longitudinal M=26 yrs, 67% white, Low SES N = 41	CAR Wake, wake +30 min, bedtime (3 days) 20, 28 & 35 weeks	ACES • No abuse: 34% • Non-sexual abuse: 44% • Sexual abuse: 21%	Daily Stress Depression Anxiety	Women with CSA displayed increased morning cortisol with prior day stress, and greater increases in evening cortisol levels in association with daily stress. Depression: No group difference	No differences in GA, BW or Apgar

Author, Year, Location	Study Design, Participants, & Sample Size	Method of Biomarker Sampling	Child Maltreatment Measures	Related Covariates	Findings	
Salivary Cortisol					**Maternal HPA Biomarker**	**Newborn Outcomes**
Shea et al., 2007 Canada	Prospective cohort M = 32 yrs, Race: not reported N = 66	CAR Wake, +30, +60 for 2 days 25-33 weeks, mean: 28.4	CTQ Continuous M = 36	Depression	Higher CTQ scores associated with lower baseline awakening cortisol.	Not reported
Walsh et al., 2016 U.S.	Prospective observational M= 17.8 yrs, 90% Latina, low SES N = 133	AUC 6 samples/day X 48 hrs 13 – 16 wks, 24 – 27 wks, 34 – 37 wks	CTQ Continuous M = 21	SCL-90 IL-6 CRP	Cortisol AUC not associated with abuse history Abuse → depression High abuse + depression →high IL-6	No effect of abuse Cortisol AUC → shorter gestation and lower BW High abuse severity + low IL-6 → shorter gestation
Plasma Cortisol						
Gillespie et al. 2017 U.S.	Prospective observational, M=26.5 yrs, 100% Black, Low SES N = 89	Single afternoon sample 28 – 32 wks M = 30.5wks	STRAIN Continuous Median = 10 Range (0 – 69)	Adult stress	Childhood stress associated w/ cortisol. No effect of adult stress	Childhood stress predicted shorter gestation, mediated by cortisol
Hair Cortisol						
Karakash et al., 2016 U.S.	Matched case-control: premature and term deliveries M=29 yrs , 38% white, 21% black N = 58	After delivery 24 to 36w5d	CTQ-SF • Abuse • No Abuse	Depression	Association between CTQ and hair cortisol not reported due to small sample size Depression: NA	Higher childhood emotional neglect → preterm birth

Author, Year, Location	Study Design, Participants, & Sample Size	Method of Biomarker Sampling	Child Maltreatment Measures	Related Covariates	Findings	
Hair Cortisol					**Maternal HPA Biomarker**	**Newborn Outcomes**
Schreier et al., 2015 U.S.	Prospective cohort M = 31 yrs, 19% Black, 46% Hispanic, varied education N = 180	All TMs After delivery	CTQ-SF • Physical/sexual • Emotional only • No abuse	PTSD	CSA and PA were associated with greater hair cortisol (while controlling for PTSD) for black women only. Depression: NA	Not reported
Schury et al., 2017 Germany	Prospective observational M=32 yrs, well educated N = 94	3rd TM only Collected M = 2 days after delivery; also collected DHEA	CTQ Continuous M = 36	Self report of depression diagnosis	CM associated DHEA in maternal hair, but not cortisol.	CM associated with higher DHEA in newborn hair
Placental Corticotrophin Releasing Hormone						
Moog et al., 2016	Prospective longitudinal, Southern California, M = 28.9 yrs, 33% white,34% Hispanic, 20% Black N = 295	Single blood draw at weeks 15, 20, 26, 30, and 37. For total of 5 samples across gestation.	CTQ No exposure: 57% One exposure: 19% 2+ exposure: 23%	Depression	CT exposure associated with 25% increase in pCRH towards end of gestation	Not reported

NOTE. M = mean; SES = socioeconomic status; TM = Trimester; EMA = Ecological Momentary Assessment; DV = domestic violence; Neg = Neglect; PA = Physical Abuse; CSA = Childhood Sexual Abuse; IPV = Intimate Partner Violence; CA = child abuse (non-sexual); GA = gestational age; BW = birth weight; CTQ = Childhood Trauma Questionnaire; CAR = cortisol awakening response; ACES = Adverse Childhood Experiences Survey; STRAIN = Stress and Adversity Inventory; CRH = Corticotrophin Releasing Hormone; CRP = C reactive protein; AUC = area under the curve

MANUSCRIPT 2

EARLY CHILDHOOD ADVERSITY, PRENATAL DEPRESSION AND THE MODERATING ROLE OF SUPPORT SEEKING ON HPA FUNCTION IN PREGNANCY

Abstract

Stress prior to and during pregnancy negatively impacts birth outcomes via complex behavioral and physiologic pathways. From a behavioral perspective, stress diminishes women's engagement in positive health behaviors during pregnancy. From a physiologic perspective, stress affects the regulation of cortisol, a hormone involved in fetal development and timing of delivery. Women use various coping styles to manage stress. It is unknown, however, whether certain coping styles attenuate the negative behavioral and physiologic effects of stress on birth outcomes. Therefore, the purpose of this descriptive, cross-sectional study was to examine the influence of coping styles on stress, physiologic cortisol regulation and health behaviors in a diverse sample of pregnant women (N=72) during the 2nd trimester. The study aims were to: 1) explain the relationship between cortisol regulation and dimensions of lifetime stress, and 2) determine whether coping moderates the effect of stress on cortisol, health behaviors, and birth outcomes. Data were collected over three prenatal visits and included self-report questionnaires, multiple salivary cortisol sampling, medical record data, and a structured stress interview. Total lifetime stress was associated with higher cortisol levels in pregnant women in the morning and evening, as well as total daily cortisol exposure. Higher morning cortisol was accounted for primarily by childhood adversity, while higher evening levels were accounted for primarily by stress and depression in adulthood. Women's willingness to seek support buffered high morning cortisol associated with childhood adversity and high evening cortisol associated with adult stress and depression. In conclusion, HPA function in pregnant women is influence by childhood adversity, adult stress and prenatal depression in unique ways, but can be buffered by willingness to seek support.

The effects of early life adversity (ELA) on multiple body systems and disease outcomes have been well established (Felitti et al., 1998). There is also some evidence that maternal ELA over the lifespan could have a programming effect on fetal development, especially neurodevelopment, which may persist into adulthood in the form of psychopathology (Seckl, 1998). Glucocorticoid over-exposure during the prenatal period is one of the primary pathways suggested to mediate maternal adversity and offspring outcomes, tested in in both humans and animals (Mustoe, Birnie, Korgan, Santo, & French, 2012; Mustoe, Taylor, Birnie, Huffman, & French, 2014; Seckl, 2008; Wadhwa, 2005). Gestational cortisol exposure has been associated with impaired fetal growth, altered stress reactivity and behavioral and affective problems during childhood (Mustoe et al., 2012; Suurland, van der Heijden, Huijbregts, van Goozen, & Swaab, 2017). The epigenetic effects of maternal adversity on the HPA axis may even be transmitted across multiple generations (Serpeloni et al., 2017).

While much has been studied about the programming effect of stress or depression that occurs during pregnancy, relatively less has been studied about programming in relation to maternal history of ELA on the gestational environment (reviewed in Manuscript 1). Childhood is a known developmental critical period during which physiologic systems are more open to environmental programming influences. ELA is associated with a variety of adverse adult health outcomes, including heart disease, cancer, lung disease, alcoholism, drug abuse, and depression, among many other leading causes of death (Felitti et al., 1998). A recent 20-year follow-up study found that childhood adversity is associated with all-cause mortality in women, but not men. The results remained even after accounting for socioeconomic status, personality traits and depression (Chen, Turiano, Mroczek & Miller 2016).

Women with the highest levels of childhood adversity are at particularly high risk (70%) for depression as adults, and are up to 12 times more likely to experience chronic recurrent depression (Brown, Craig, Harris, Handley, & Harvey, 2007) with an unfavorable course of illness that is less likely to respond or remit to treatment (including therapy, medication or both) (Nanni, Uher, & Danese, 2012). Maternal depression may also mediate the association between maternal early exposure to adversity and later behavioral problems in her offspring (Miranda, de la Osa, Granero, & Ezpeleta, 2013). Women who were abused as children are more likely to have depression, which partially, if not fully, mediates the relationship between maternal childhood maltreatment and offspring externalizing disorders.

In addition to environmental factors, depression is influenced by genetic factors, possibly through a gene-environment interaction. Individuals may be more or less likely to develop depression based on genetic polymorphisms and prior experience. One study found that polymorphism in the 5-HTTLPR increases susceptibility to stress towards depression, with the strongest moderation effect from child maltreatment and less so for stressful life events in adulthood (Karg, Burmeister, Shedden, & Sen, 2011). Other genes have also been found to mediate the relationship between childhood adversity and cortisol stress reactivity in adulthood, providing evidence for the epigenetic basis of differential susceptibility to stress reactivity (Houtepen et al., 2016). Some have suggested that disorders occurring in individuals who experienced childhood maltreatment may be biologically distinct from disorders that occur in individuals without childhood maltreatment (Shalev, Heim, & Noll, 2016).

Fetal programming was originally thought to be relatively stable and persist into adulthood, regardless of environmental or social buffering. Several human and animal studies have provided evidence that social environment may have a more substantial buffering effect than originally assumed. Some animal studies have shown that social factors in the post-natal context

can buffer HPA reactivity that was programmed earlier through gestational cortisol exposure or early adversity (Francis, Diorio, Plotsky, & Meaney, 2002; Morley-Fletcher, Rea, Maccari, & Laviola, 2003; Mustoe et al., 2014). Less has been reported on whether human maternal willingness to actively seek social support or use of specific individual coping strategies attenuate elevated stress reactivity.

Behavioral factors have also been documented as potential mediators between maternal stress and glucocorticoid-related programming effects on the fetus. Behavioral mediators include health behaviors known to be associated with pregnancy outcomes such as diet, exercise, smoking and substance use. Maternal unbalanced diet has been found to lead to long-lasting epigenetic modifications in HPA-associated genes, such as methylation of the glucocorticoid receptor gene. This was found to be the case in middle aged women whose mothers had unbalanced diets during pregnancy (Drake et al., 2012). Diets high in sugar and fat during pregnancy have been associated with epigenetic modifications in genes (IGF2) that are involved in fetal brain development. This study also found a subsequent increased risk for attention deficit hyperactivity disorder for offspring in childhood associated with maternal diet during pregnancy (Rijlaarsdam et al., 2017). In a large population study (N = 7,511) of pregnant women's adherence to national dietary guidelines, women who had less than a college degree, or were non-Hispanic Black or Hispanic were more likely to have poor diet quality, with 34% of energy being consumed from empty calories (Bodnar, Simhan, Parker, & Meier, 2017). These groups of women are also much more likely to experience higher levels of lifetime adversity and stress.

Purpose

The purpose of this study is to 1) describe how dimensions of lifetime stress relate to cortisol regulation during pregnancy, and 2) determine whether coping moderates the relationships between stress and a) health behaviors, b) cortisol and c) birth outcomes (see conceptual model in Figure 1 in the introduction section).

Methods

Participants

A convenience sample of 75 pregnant women was recruited from a hospital-based women's health clinic in a Midwestern urban city. Eligible participants were women age 19 to 45 with a single intrauterine pregnancy between 20 and 28 weeks gestation, able to read / speak English and able to be reached by telephone or text. Women were excluded if they had received a referral for care in the high-risk pregnancy clinic, had major pregnancy complications or existing medical issues prior to recruitment (i.e. cervical or uterine abnormalities, renal, hepatic or cardiac disorders, insulin-dependent diabetes, preeclampsia, regular oral steroid use in the month prior to data collection, diagnosed congenital fetal abnormalities, active placenta previa, or other disorders/medication use that could affect cortisol levels). Women were also excluded if they regularly worked night-shift. Two participants voluntarily dropped out from the study, and one was lost to follow-up. The final sample included 72 women.

Procedure

The study was a mixed-methods convergent design. The data were collected prospectively, and only the quantitative data results are discussed here. The qualitative data is discussed in Chapter 3. The study was approved by the university's Institutional Review Board (Letter of approval in Appendix A). Potential participants were recruited at a routine prenatal visit (study

recruitment flyer Appendix B). Written informed consent was obtained from all participants. Pregnant women completed one to three study visits during the second half of pregnancy. On the first visit participants were consented, given a packet of questionnaires (description of measures Appendix C) to complete and were provided verbal, visual and written instructions on saliva collection. Participants were emailed a link to complete the online stress assessment. Participants collected a total of 15 saliva samples using cotton Salivettes over three days. They were instructed to collect saliva at awakening, 30 minutes after awakening, during the early afternoon, evening, and bedtime. They also completed a saliva sampling log, including the time of sampling, and questions about daily stress and sleep. Research staff stressed the importance of accurate timing of collection and avoidance of activities that could affect salivary cortisol levels in the half hour prior to collection (i.e. eating, exercise, smoking, caffeine). Participants were instructed to freeze their saliva samples in a home refrigerator until sampling was complete. They were instructed to then return the samples via postal mail in a stamped, pre-addressed envelope that was provided to them or return the samples at the next study visit two to four weeks later. Salivary cortisol has been shown to remain stable refrigerated for at least 3 months and is unaffected by repeated cycles of thawing and freezing (Garde & Hansen, 2005). At the second visit participants completed the STRAIN in the clinic, if not already completed. Participants were given honorariums for each study activity completed, up to a total of $95.

Measurement of Variables

Stress. The Stress and Adversity Inventory (STRAIN) is an online stress assessment administered using computerized intelligent logic to assess 96 different stressors (66 acute life events and 30 chronic difficulties) occurring over an individual's lifetime (Slavich & Epel, 2010). There are 220 potential items, and items irrelevant to the individual are automatically omitted. The STRAIN assesses each stressor's severity, frequency, timing (childhood <18 yrs vs. adulthood

>18 yrs), and duration (acute vs. chronic), covering 14 major life domains (housing, education, work, etc.) and five social-psychological characteristics (interpersonal loss, physical danger, humiliation, entrapment, role change) (see list in Table 2). Summed scoring was used for stress exposure (0 to 96) and severity (0 to 480), with higher scores representing higher stressor count and severity, respectively. The validity of this question set has been examined in over 10,000 participants from 32 studies spanning several populations and all age groups, with predictive validity for a range of physical and mental health symptoms, including depression. Criterion validity is established from the development of the question set being based on the gold-standard interview system for assessing life stress, the Life Events and Difficulties Schedule (Brown & Harris, 1978). The STRAIN was developed by a team of experts trained in this gold-standard method. Lifetime stress (STRAIN) was examined in relation to cortisol parameters first as a cumulative lifetime score, and second in relation to timing, duration, perceived severity and characteristic of the stress (Table 2).

Table 2. Sub-scales of the STRAIN by dimension of stress

Timing[1]	Duration	Domain	Characteristic
Childhood	Acute	Housing	Loss/Relational Disruption
Adulthood	Chronic	Education	Danger (Physical)
		Work	Humiliation
		Treatment/Health	Entrapment
		Marital/Partner	Role Change/ Disruption
		Childhood/Early Adversity	
		Reproduction	
		Financial	
		Legal/Crime	
		Other Relationships	
		Death	
		Life Threatening Situation	
		Accident	
		Possessions	

Note. [1] The cutoff for timing of stress is 18 years of age.

Depression. The Edinburgh Postnatal Depression Scale (EPDS) (Appendix D) is a 10-item self-report scale evaluating depressive symptoms over the last 7 days, rated on a 4-point scale from zero (no, not at all) to three (yes, most of the time) (Cox, Holden, & Sagovsky, 1987). Summed scores range from 0 to 30, with higher scores indicating greater severity of depressive symptoms. A cutoff score of 10 or greater has shown good sensitivity (70%), specificity (96%) and positive predictive value (39%) in pregnant women during the 2nd trimester for depression. Internal consistency reliability was α=0.83, and test-retest reliability was r = 0.63. Concurrent validity (Symptom Checklist 90) and predictive criterion validity (CIDI-depression) have also been established (Bergink et al., 2011; Cox et al., 1987). Prior studies have indicated that use of this tool as a dichotomous variable, rather than continuous scale, provides more robust and clinically meaningful findings (Grote et al., 2010). Depression was considered a dimension of lifetime stress, representing the cognitive / emotional response to life stress and adversity.

Coping. The Brief COPE (Appendix D) is a 28-item scale evaluating how frequently an individual uses coping strategies on a 4-point scale ranging from one (I haven't been doing this at all) to four (I've been doing this a lot) (Carver, 1997). Scores are summed, ranging from two to eight for each of the 14 subscales (active coping, planning, reframing, accepting, humor, religion/spirituality, seeking emotional support, seeking instrumental support, distraction, denial, venting, substance use, disengagement, and self-blame). Two factors have previously been identified in pregnant women, including active (α = 0.86) and disengaged (α = 0.78) coping (Ruiz et al., 2015). The scale has demonstrated convergent and discriminant validity (Carver, 1997). The Brief COPE was derived from a larger coping inventory previously developed by the same authors (Carver, Scheier, & Weintraub, 1989).

Health Behaviors. The Health Practices in Pregnancy Questionnaire-II (HPQ-II) (Appendix D) is a 34-item self-report questionnaire addressing health practices known to affect pregnancy outcomes in six areas (balance of rest and exercise, safety measures, nutrition, avoiding use of harmful substances, obtaining health care, and obtaining information) (Lindgren, 2005). Responses range from one (never) to five (always or daily), and summed scores range from 34-170. Higher scores indicate better health practices. The scale has internal consistency reliability in previous pregnant samples ($\alpha = 0.81$) and content and construct validity (Lindgren, 2005).

Electronic Medical Record. Weight gain (considered a proxy for healthy diet and exercise) was calculated based on the IOM (Yaktine & Rasmussen, 2009) pregnancy weight gain recommendations, and were determined using the first and last prenatal visit weight, and adjusting for weeks of gestation at the time of weighing. The adequacy of prenatal care utilization (APNCU) is a two-factor index based on time of prenatal care initiation and number of prenatal care visits received based on week of gestation (Kotelchuck, 1994). Inadequate care is defined as later initiation of prenatal care and less than the recommended number of prenatal visits, accounting for when care was initiated. Prenatal care is evaluated as inadequate, intermediate, adequate and adequate plus. Birth outcome data (length of gestation, birth weight, birth length, head circumference, and Apgar scores) were extracted from the electronic medical record (EMR). Other data collected from the EMR included race, ethnicity, prenatal care and pregnancy information, delivery outcomes and complications, medical and medication history.

Cortisol Processing. Returned saliva samples were stored in a locked freezer at -23° C until processing. Samples were processed in duplicate at the University of Nebraska at Omaha (UNO) Endocrine Bioservices Laboratory by enzyme immunoassay (EIA). Microtiter plates were coated with anticortisol antibody [R4866, raised against a steroid bovine albumin (BSA) in rabbit] and

incubated overnight. Saliva samples were thawed, vortexed and centrifuged at 2,000 rpm for 5 minutes. After centrifugation 100 mL of the supernatant of the sample was extracted and diluted with 100 mL of double-distilled water for a 1:2 dilution. Diluted samples (50 mL) were assayed in duplicate on plates along with known cortisol standards. Labeled cortisol (horseradish peroxidase) was added to wells during a two-hour incubation. After separation of free from bound cortisol, substrate (hydrogen peroxide and 2,2azino-bis(3)-ethylbenzthiazoline-6-sulphonic acid) was added to each well, and absorbance was measured approximately 1 hour after incubation. A four-parameter sigmoid fit regression was used to calculate cortisol concentration values. These concentrations were adjusted to values expressed as ng/ml. Duplicate cortisol values that varied by more than 20% were re-assayed. A quality control sample of pooled saliva was assayed on each plate, and the intra- and inter-assay coefficients of variation were less than 10% and 15% respectively.

Statistical Analysis

Power analysis. The sample size for Aim 1 was determined using G*power (Faul, Erdfelder, Buchner, & Lang, 2009), with an effect sizes of r = 0.35. The analysis indicated that a correlational bivariate model for a two-tailed test ($\alpha = 0.05$, power: 0.8) would require a sample size of 61 women for a fully powered study for Aim 1. We oversampled to account for 20% attrition, requiring a total sample size of 75. For Aim 2, general linear modeling was utilized. In a multiple regression model with three predictors (two main effects and an interaction), the planned final sample size of 61 gives sufficient power to detect significance in a regression coefficient with an effect size of $f^2 = .191$, which is a medium effect size.

Outliers and transformation of non-normal variables. Data from 72 pregnant women were used in the analysis and examined for outliers and distribution (see list of study variables, Appendix E). No outliers were excluded. All variables were examined for non-normal

distribution, skew, and kurtosis by a) Shapiro-Wilks test (rejecting null-hypothesis, $p < .05$), b) z-scores for skew and kurtosis ($z > 2$) and c) visual examination of a histogram (see Appendix F for tests of normality). The variables that required transformation were cortisol, length of gestation, EPDS and the STRAIN scales. Average cortisol values for each collection time point were natural log transformed. Depression scores were natural log transformed. Length of gestation was transformed by subtracting 231 (1 less than the lowest value) and squaring all values. Finally, STRAIN variables were transformed using square root. All transformed variables were examined again to ensure normality following transformation.

Determination of covariates. Correlation tables between all groups of variables were examined (i.e. demographics, stress, cortisol, self-report measures, and birth outcomes). The correlations between outcome variables and demographic variables were examined, and variables with the most robust correlations were considered for inclusion as covariates. Other covariates that were considered for inclusion, based on prior studies included gestational age at cortisol collection, smoking, pre-pregnancy BMI, and history of preterm birth. Step-wise linear regression was then performed using each main variable as the outcome (i.e. stress, depression, cortisol, coping, and birth outcomes) to aid in deciding which variables to use as covariates in the analyses.

Partial Pearson correlations were used for normal distributions, while partial Spearman correlations were used for non-normal distributions (Supplementary tables in Appendix G). Cortisol awakening response (CAR), diurnal slope, and area under the curve with respect to ground (AUCg) were calculated from averaged values over the three days. AUGg was determined based on the trapezoid formula described by Pruessner et al. (2003). Partial Spearman correlation analyses were used for non-normal distributions. Prior studies have found that approximately 30% of adult women experience sexual and/or physical abuse as a child

(Records & Rice, 2009; Stoltenborgh, Bakermans-Kranenburg, Alink, & IJzendoorn, 2015). Therefore, for this study, a cutoff ratio of 30:70 was used for high and low stress for the purposes of moderator analysis and graphs.

General linear modeling was performed (using all available data) to determine the role of coping as a moderator. Variables demonstrating significant effects or sizable effect sizes were plotted onto an interaction plot to facilitate interpretation. SPSS v. 23 software was used for all statistical analyses.

Results

Descriptive statistics for the sample are listed in Table 3. Overall, the sample was diverse across most demographic variables. The mean age was 28.4 years (SD = 5.3 years). The sample was 60% non-Hispanic White, 19% Black or African American, and 11% Hispanic (other races are listed in Table 3). Roughly half of the sample had at least an associate's degree (52%), were married (54%), low income (53%) (annual household income less than $40,000), insured by Medicaid (46%), and nulliparous (46%). The average pre-pregnancy body mass index (BMI) was 27.9, which is considered overweight. Women were, on average, 27 weeks pregnant at the time of cortisol sampling, which aligns with the end of the 2nd trimester. There was a relatively narrow timeframe for cortisol collection (SD = 17 days), which served to minimize the variability in cortisol as gestation advanced. The average length of gestation was 275.6 days (SD = 11 days) or 39.4 weeks. Nearly one-third (31%) of women scored 10 or higher on the EPDS, indicating possible presence of depression. This rate is substantially higher than rates (%14) of depression documented in nationally representative samples of reproductive-aged women (Farr, Bitsko, Hayes, & Dietz, 2010). Descriptive statistics for the eight cortisol parameters included in analyses are listed in Table 4. These parameters include the five collection times (awake, awake

+30, afternoon, evening, bedtime) and diurnal characteristics (CAR, slope and AUCg). A line graph of the average cortisol values across all participants is shown in Figure 3.

Covariates

The demographic variables of age, income and non-White race/ethnicity showed the most robust correlations across all categories of variables and were therefore inputted for step-wise linear regression. Smoking was also correlated with stress and cortisol variables and considered in regression for inclusion as a covariate for aim 1. Gestational age at cortisol collection, pre-pregnancy BMI, and history of preterm birth were not correlated with the predictors or outcomes and therefore not considered for the regression model.

The next step in determining covariates was to use step-wise linear regression to identify confounding factors for each major variable (stress, birth outcomes, cortisol, depression and coping). Consistent covariates were used for each section of analysis. When total lifetime stress was entered as an outcome, income was indicated as a covariate (R^2 = .16, F (1,62) = 11.30, p<.01; β = .40, p<.01). When childhood adversity was entered as an outcome, age was indicated as a covariate (R^2 = .08, F (1,62) = 5.42, p=.02; β = -.286, p=.02). When adult stress was entered as an outcome, smoking and income (R^2 = .20, F (1,62) = 7.48, p=.001; β [smoke] = .31, p=.01; β [income] = .25, p = .04) were indicated as covariates. When bedtime cortisol was entered as an outcome, age and smoking were indicated as covariates (R^2 = .22, F (1,63) = 8.52, p=.001; β [age] = -.35, p=.003; β [smoke] = .34, p = .004). When slope was entered as the outcomes, age and smoking were indicated as covariates (R^2 = .20, F (1,63) = 7.76, p=.001; β [age] = -.37, p=.002; β [smoke] = .28, p = .02). When depression was entered as the outcome, income was indicated as a covariate (R^2 = .09, F (1,62) = 5.90, p=.02; β = .30, p = .02). When length of gestation was entered as an outcome, non-White as indicated as a covariate (R^2 = .09, F (1,61) = 5.60, p = .02; β

= -.29, p = .02). No covariates were indicated for awakening, 30 minutes post-awakening, afternoon, or evening cortisol. Covariates were also not indicated when CAR, AUCg or coping were entered as the outcome.

Based on the results of the step-wise linear regression, the covariates for analyses involving stress and cortisol were age and smoking. For analyses involving length of gestation as the outcome, covariates were age, income, smoking and non-White.

Table 3. *Participant Characteristics*

Participant (N=72) Characteristic	Frequency (%)	Mean ± SD
Maternal Age		28.4 yrs (5.3)
Maternal Race		
White	44 (60%)	
Black or African American	14 (19%)	
Asian	5 (7%)	
Native Hawaiian and Other Pacific Islander	1 (1%)	
American Indian and Alaska Native	1 (1%)	
Other	8 (11%)	
Hispanic Ethnicity	7 (10%)	
Completed college (associates or higher)	35 (52%)	
Unemployed, seeking work	10 (15%)	
Married	39 (54%)	
Low Income[1]	35 (53%)	
Insured by Medicaid	33 (46%)	
Nulliparous	33 (46%)	
History of preterm birth	5 (7%)	
Pre-Pregnancy BMI		27.9 (6.7)
Gestational age at cortisol collection		188.0 (17) d / 27 wks
Length of Gestation (days / weeks)		275.6 (11.0) d / 39.4 wks
Birth Weight		3416.8 g (495.5)
Depression[2]	22 (31%)	7.5 (48.8)

Note. EPDS = Edinburgh Postnatal Depression Scale

[1] Low Income = Annual household income less than $40,000

[2] Depression was used as a dichotomous variable using a cutoff of 10 or greater on the EPDS

Table 4. *Descriptive statistics: Cortisol*

Cortisol parameter (n = 67)	Minimum	Maximum	Mean	SD
Collection times				
Awake	3.43	38.05	11.16	5.29
Awake +30 min	3.47	41.30	13.14	5.19
Afternoon (~12:30 p.m.)	2.53	15.20	7.10	2.92
Evening (~6:30 p.m.)	1.60	13.67	4.60	2.20
Bedtime (~10:30 p.m.)	1.37	10.40	3.52	1.65
Diurnal characteristics				
Cortisol awakening response (CAR)[1]	-19.78	18.10	1.98	4.56
Slope[2]	-2.16	0.14	-0.53	0.35
AUCground[3]	2357	15643	6221	2194

Note. Table describes non-transformed cortisol values, averaged across three days of collection.
[1]CAR = Awake + 30 – Awake
[2]Slope = (Awake – Bedtime) / hours awake
[3]AUCground was calculated using the trapezoid formula including all 5 collection times.

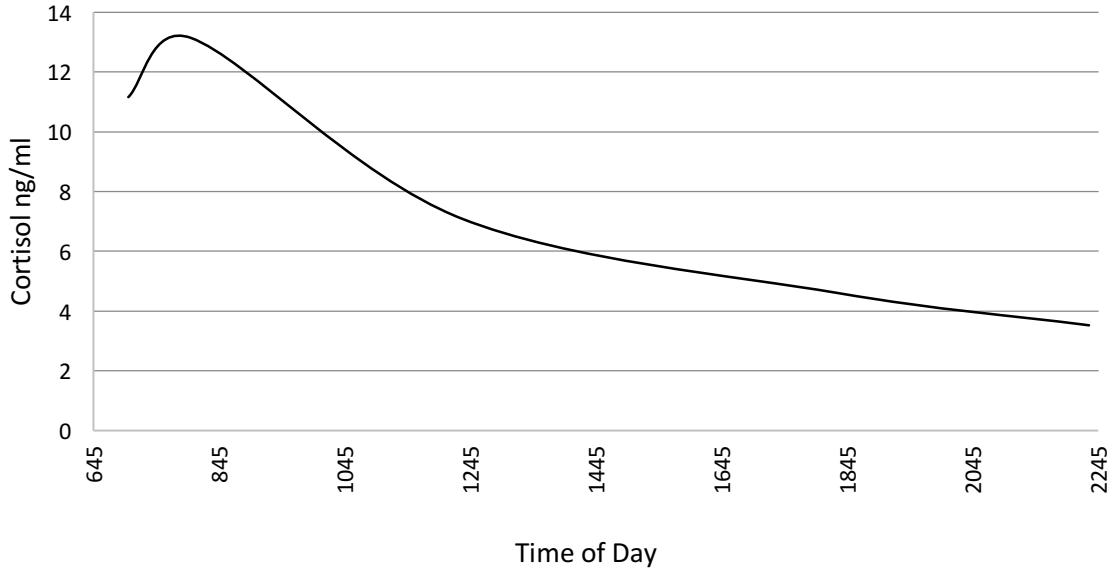

Figure 3. Diurnal cortisol trajectory.
This line graph depicts the diurnal cortisol trajectory averaged across the entire sample (N = 67).

Table 5. Dimensions of lifetime stress and cortisol: Partial Pearson correlations

Total Stress Count	Awake	Awake +30 min	Afternoon (~12:30 p.m.)	Evening (~6:30 p.m.)	Bedtime (~10:30 p.m.)	CAR	Slope awake to bedtime	AUCg
Lifetime Stress Total	.10	.33*	.03	.16	.18	.12	-.04	.22
Timing								
Early Adversity	.22	.44*	.06	.09	-.06	.25	-.24	.20
Adulthood	.01	.20	-.03	.10	.17	.01	.05	.12
Duration								
Acute	.07	.33*	.07	.17	.24	.12	.00	.24
Chronic	.05	.27*	-.02	.11	.05	.16	-.01	.15
Domain								
Housing	-.03	.24	.00	.19	.22	.25	.11	.15
Education	.13	.17	-.06	-.03	-.05	.05	-.14	.05
Work	-.05	-.06	-.12	-.09	-.03	-.09	.00	-.11
Treatment/Health	.15	.36*	.03	.06	.10	.12	-.14	.21
Marital/Partner	.06	.03	-.09	-.02	.01	-.19	.00	.01
Reproduction	-.15	-.12	-.25	-.26*	-.16	.05	.14	-.14
Financial	.04	.21	.17	.31*	.26*	.14	.02	.24
Legal/Crime	-.20	.03	.00	.05	.03	.12	.24	.04
Other Relationships	.05	.23	.02	.15	.15	.16	.03	.16
Death	-.03	.15	.10	.20	.17	.09	.05	.18
Life-Threatening Situations	.16	.20	.02	-.01	-.01	-.07	-.15	.09
Possessions	.08	.16	.02	.18	.23	.09	.07	.18
Characteristic								
Interpersonal Loss	.01	.18	-.02	.16	.14	.01	.04	.14
Physical Danger	.15	.32*	-.02	.04	.18	.04	-.10	.19
Humiliation	.02	.21	-.01	.12	.18	.10	.08	.13
Entrapment	.17	.22	.13	.24	.13	.07	-.14	.23
Role Change/ Reversal	-.01	.29*	.08	.14	.06	.26*	.06	.17

Note. Each stress variable is a count of events or difficulties experienced within each category. The transformed values of the stress scales and cortisol parameters were used in this analysis. Analysis controlled for age, income & non-Hispanic White.

* $p < .05$

Lifetime stress and cortisol

Partial Pearson correlations are listed in Table 5 including all eight cortisol parameters with each of the dimensions of the STRAIN scale. The majority of significant correlations were with the post-30 minute awakening sample.

There was a statistically significant difference in maternal cortisol based on prior history of lifetime stress, $F(7, 54) = 2.245$, $p = .04$; Wilks' $\Lambda = .775$, $\eta = .225$. In GLM analysis controlling for age and smoking, total lifetime stress was associated with higher cortisol at 30 minutes after awakening ($p<.01$), evening ($p=.03$), and higher AUCg ($p=.04$). The line graph in Figure 4 shows a pattern for higher cortisol across the entire day for women who have experienced higher stress over their lifetime.

Timing of Stress

The timing of stress (adult vs. childhood) was differentially associated with cortisol during pregnancy. There was not a statistically significant difference in maternal cortisol based on prior history of adult stress, $F(7, 53) = .807$, $p < .585$; Wilks' $\Lambda = .904$, $\eta = .096$. In a GLM analysis controlling for age, smoking and childhood adversity, stress occurring in adulthood did not predict any cortisol parameters (Figure 5). However, in an independent t-test, cortisol was significantly higher in the evening ($M = 5.61$, $SD = 2.46$) for women with high adult stress compared to women with low adult stress ($M = 4.27$, $SD = 2.04$, $t(62)= -2.24$, $p=.03$) and at bedtime (high stress $M = 4.53$, $SD = 2.37$; low stress $M = 3.18$, $SD = 1.13$, $t(62) = -2.31$, $p=.03$).

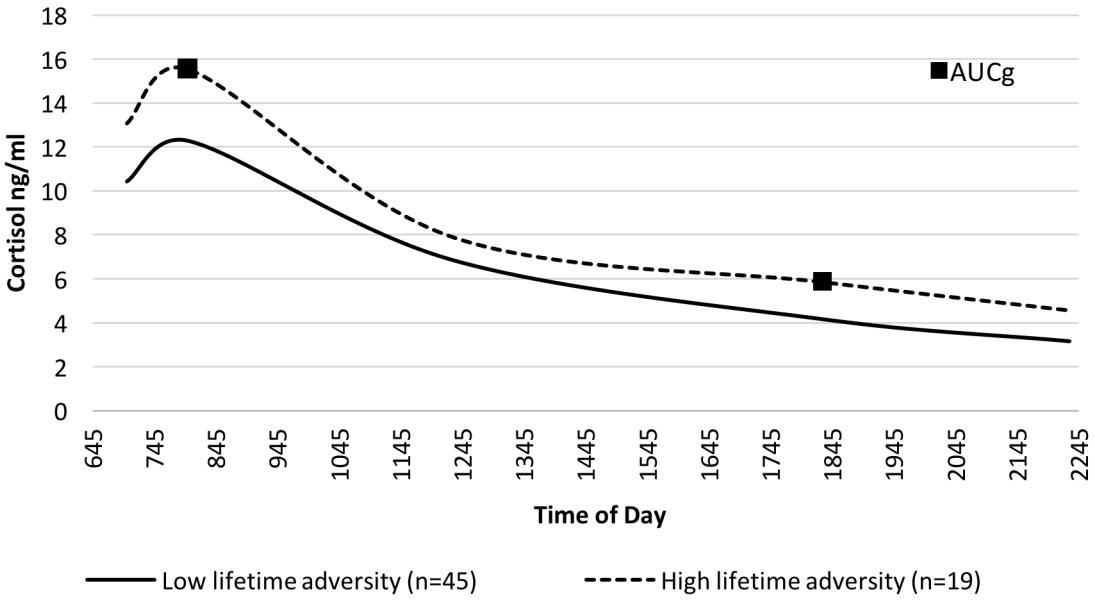

Figure 4. Lifetime stress: comparison of diurnal cortisol trajectory in women with high vs. low lifetime stress.
Lines represent total lifetime stress count cut at a 30:70 ratio. Women with high lifetime stress show a pattern of elevated cortisol secretion. ■ GLM $p \leq .05$

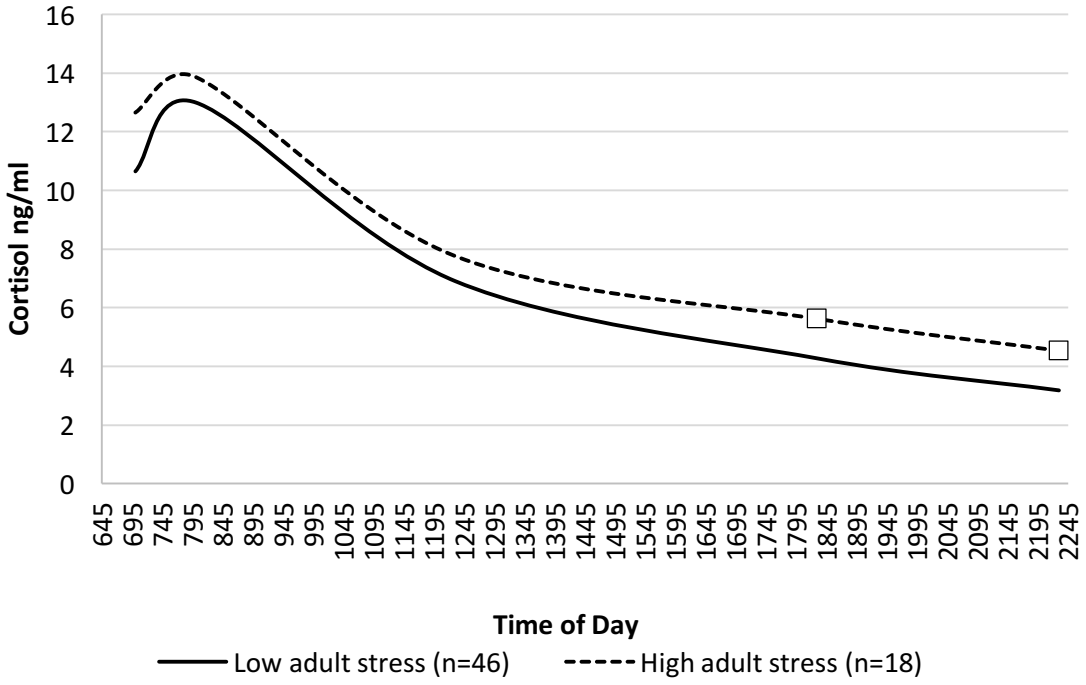

Figure 5. Adult stress: comparison of diurnal cortisol trajectory between women with low vs. high adult stress.
Lines represent adult stress cut at a 30:70 ratio. Women with high adult stress show a pattern of elevated evening and bedtime cortisol. □ t-test $p \leq .05$

Next, the relationship between childhood adversity was tested. There was a statistically significant difference in maternal cortisol based on prior history of childhood adversity, $F(7, 53) = 3.917$, $p < .002$; Wilks' $\Lambda = .659$, $\eta = .341$. In GLM controlling for age, smoking and adult stress, childhood adversity predicted higher cortisol at awakening ($p = .05$, $\eta = .064$), 30 minutes after awakening ($p < .01$, $\eta = .282$), as well as a larger CAR ($p = .03$, $\eta = .076$) (Figure 6).

Childhood Adversity Moderates Response to Stress in Adulthood

Next we examined whether women's cortisol response to adult stress differed based on whether they experienced childhood adversity. After controlling for age, smoking and main effects, there was not a statistically significant interaction between adult stress and childhood adversity across all cortisol parameters together, $F(7, 52) = 1.545$, $p = .173$; Wilks' $\Lambda = .828$, $\eta = .172$. However, there were statistically significant interactions between childhood adversity and adult stress on slope $F(1,58) = 5.841$, $p = .02$, $\eta = .09$.

In order to determine whether the interaction was due to morning or evening cortisol levels, the data were split based on high and low childhood adversity scores. Figures 7 and 8 illustrate the diurnal cortisol trajectory with graphs representing low and high childhood adversity and lines representing low and high adult stress. Separate GLM models were then run for each group (i.e. high and low childhood adversity) including age, smoking, and adult stress. Among women with low childhood adversity (n=46), high adult stress predicted higher evening ($p = .05$, $\eta = .128$) and bedtime cortisol ($p = .02$, $\eta = .121$), and a flatter slope ($p = .02$, $\eta = .093$) (Figure 7). This pattern was not true for women who experienced high child adversity (n=18), in which adult stress did not predict any cortisol parameters (Figure 8).

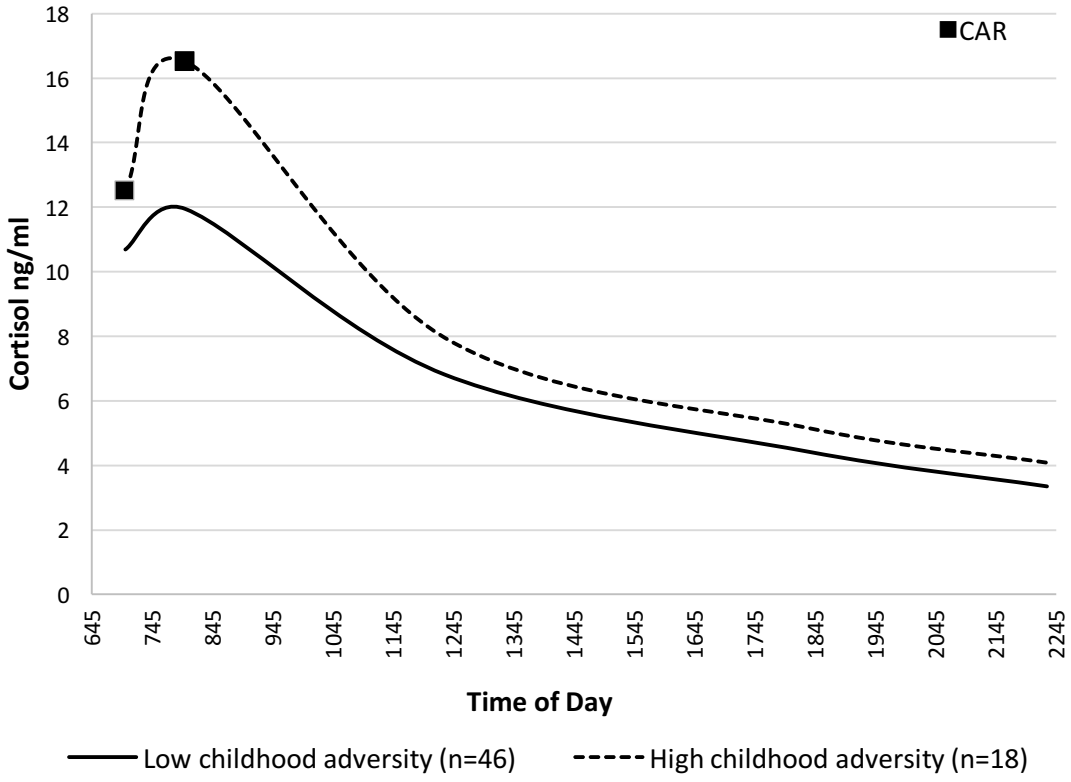

Figure 6. Childhood adversity: comparison of diurnal cortisol trajectory in women with a history of low vs. high childhood adversity.
Controlling for age, smoking and adult stress. Lines represent child adversity scale cut at a 30:70 ratio. Women with high childhood adversity have elevated morning cortisol levels and CAR. ■ GLM $p \leq .05$

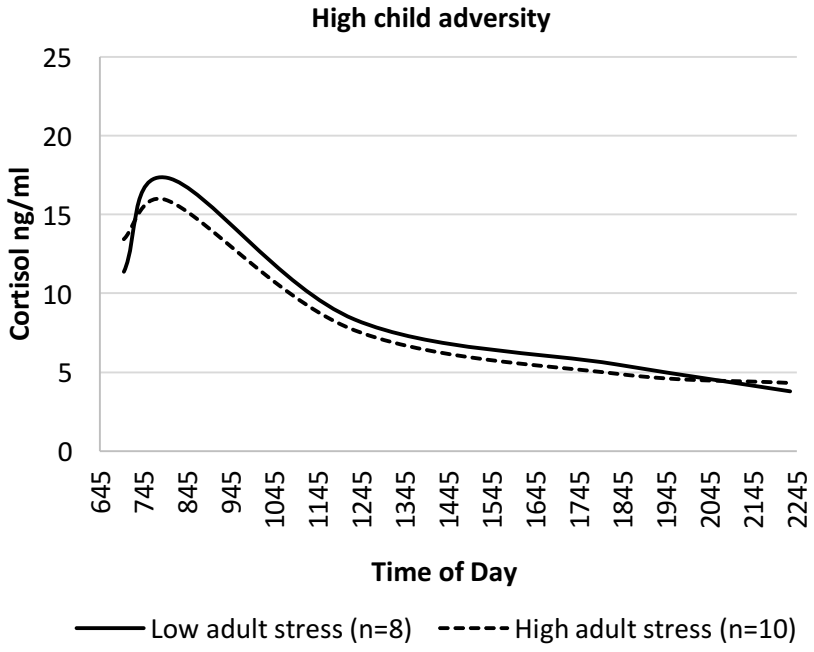

Figure 7. High childhood adversity and adult stress: Comparison of diurnal cortisol trajectory between women with high and low adult stress.
Lines representing low and high adult stress. There are no differences between groups.

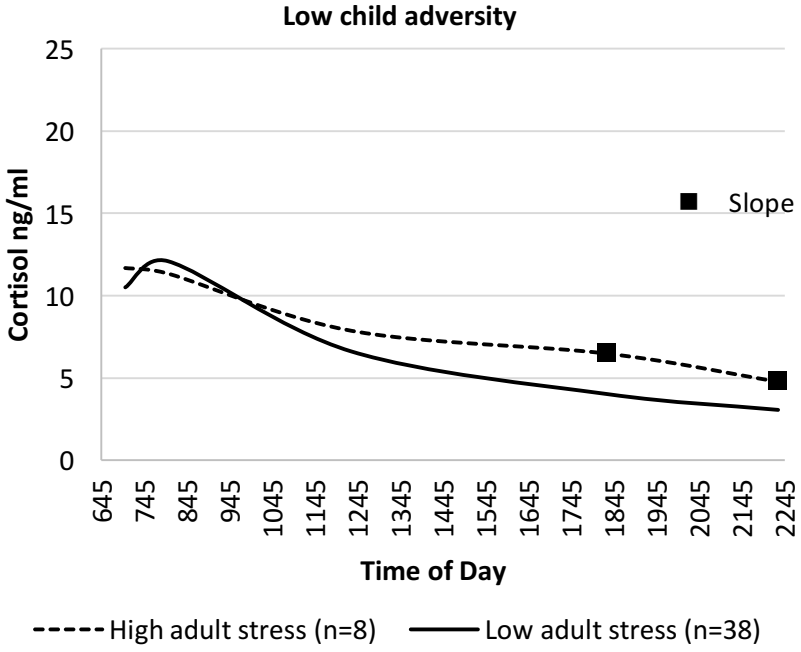

Figure 8. Low child adversity: Comparison of diurnal cortisol trajectory between women with high and low adult stress. Women with high adult stress show a pattern of elevated evening and bedtime cortisol. Lines representing low and high adult stress.
■ GLM $p \leq .05$

Prenatal Depression

Prenatal depression is considered here to be an aspect of lifetime stress, or more specificially, distress. While the STRAIN counts the number and severity of stressful events or difficulties experienced, depression can be viewed as the cognitive and emotional response to cumulative stress. Women with high childhood adversity were 5 times more likely to score 10 or greater on the EPDS (OR = 5.1), with 58% of those with ELA scoring at or above this cutoff. There was statistically significant difference in maternal cortisol based on depression, $F(7, 56) = 2.344$, $p < .036$; Wilks' $\Lambda = .773$, $\eta = .227$. In GLM analysis, controlling for age and smoking, prenatal depression (score 10 or greater on the EPDS) was associated with cortisol at awakening ($p<.01$, $\eta = .139$), a smaller CAR ($p=.01$, $\eta = .097$), and greater AUCg ($p=.03$, $\eta = .071$) (Figure 9). These associations were significant only when depression was inputted as a dichotomouse (as opposed to continuous linear) variable.

Childhood Adversity Moderates HPA function in Depression

Since childhood adversity moderated the relationship between adult stress and cortisol, childhood adversity was also examined as a moderator between prenatal depression and cortisol. Using GLM, which controlled for age and smoking, the interaction between childhood adversity and prenatal depression was statistically significant for cortisol levels at bedtime, $F(5,58) = 4.04$, $p=.049$, $\eta = .065$) and on slope, $F(5,58)$, $p=.03$, $\eta = .082$). The data were split between women with high and low childhood adversity and then the effects of depression were tested in GLM while controlling for age and smoking. Among women with high childhood adversity, there were no associations between depression and any of the cortisol parameters (Figure 10). Among women who experienced low childhood adversity, depression was associated with higher cortisol at awakening, $F(3,42) = 7.35$, $p =.01$, $\eta = .149$, and an inverted CAR, $F(3,42) = 11.16$, $p < .01$, $\eta = .21$ (Figure 11). Figure 12 displays all four groups in one line

graph for comparison. In an interaction plot (Figure 13), women without childhood adversity showed greater increases in bedtime cortisol as depressive symptoms increased.

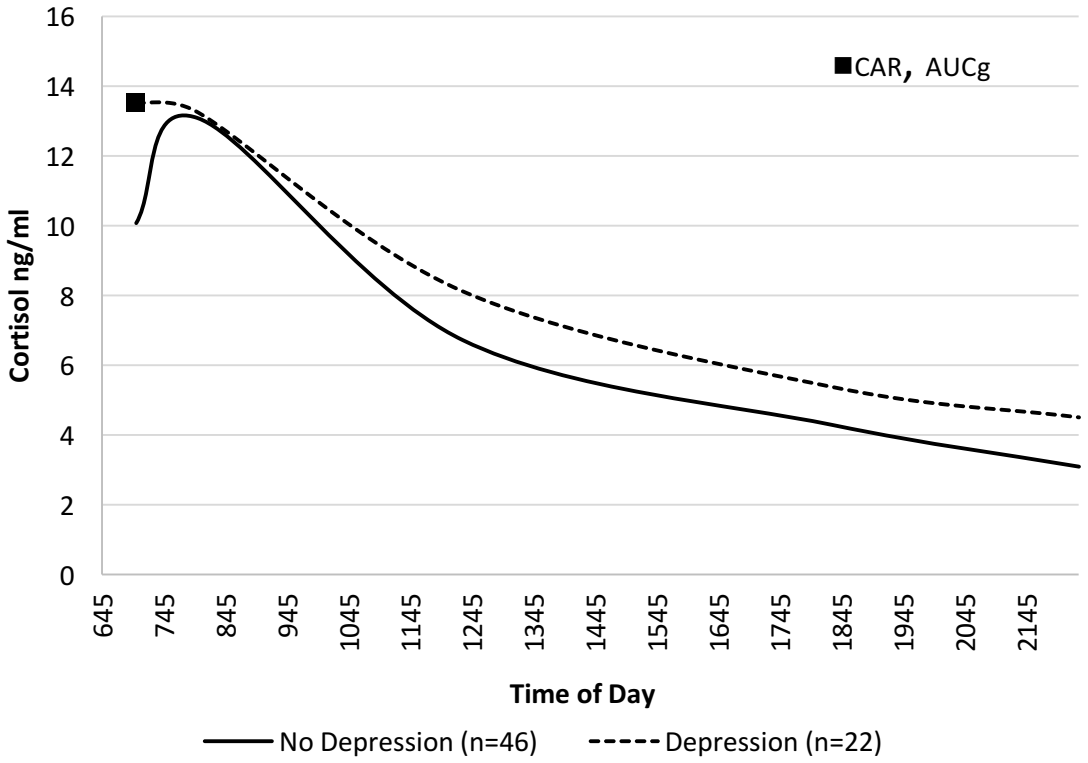

Figure 9. Depression: Comparison of diurnal cortisol trajectory in women with and without depression.
Cut score EPDS ≥ 10. Depressed women have a flat CAR, and higher total cortisol over the day.
■ GLM $p \leq .05$

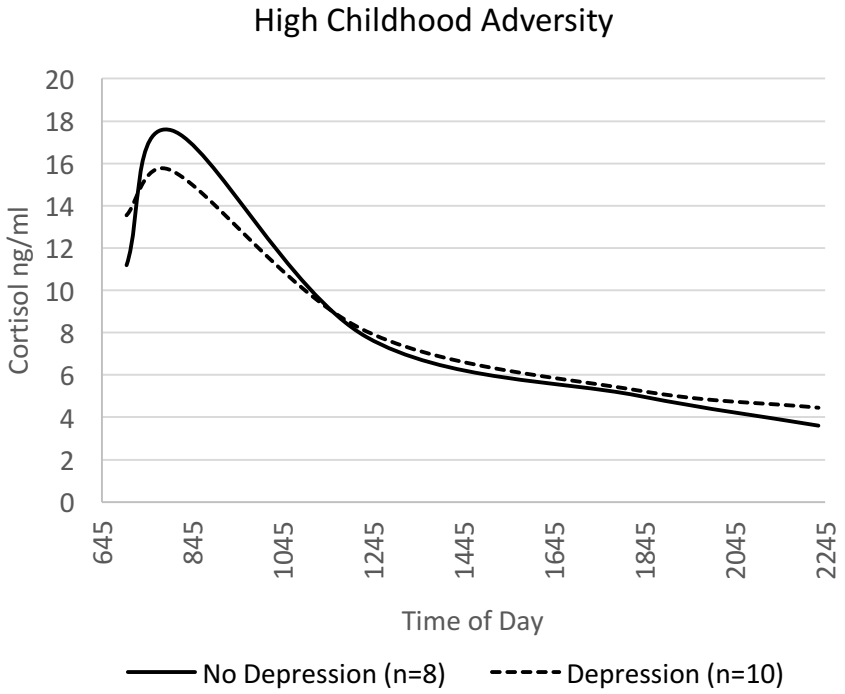

Figure 10. High childhood adversity and depression.
Comparison of diurnal cortisol trajectory in sub-sample of women who experienced high childhood adversity and either depressed or not depressed. Lines represent depression and no depression. There are no differences between groups.

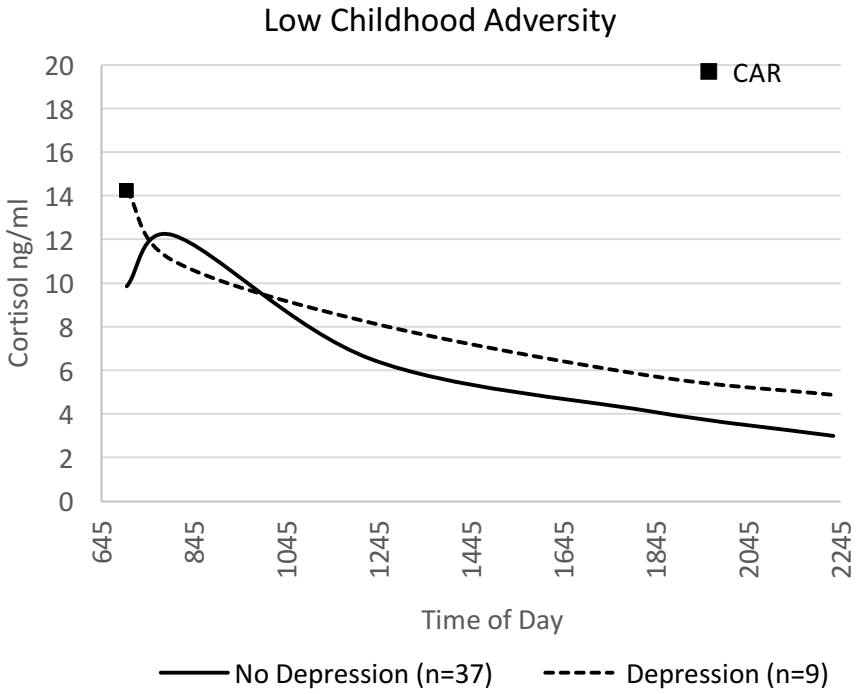

Figure 11. Low childhood adversity and depression.
Comparison of diurnal cortisol trajectory in sub-sample of women who experienced low childhood adversity and either depressed or not depressed. Lines representing depression and no depression. Depressed women have a negative CAR, and pattern for higher evening cortisol. ■ GLM $p \leq .05$

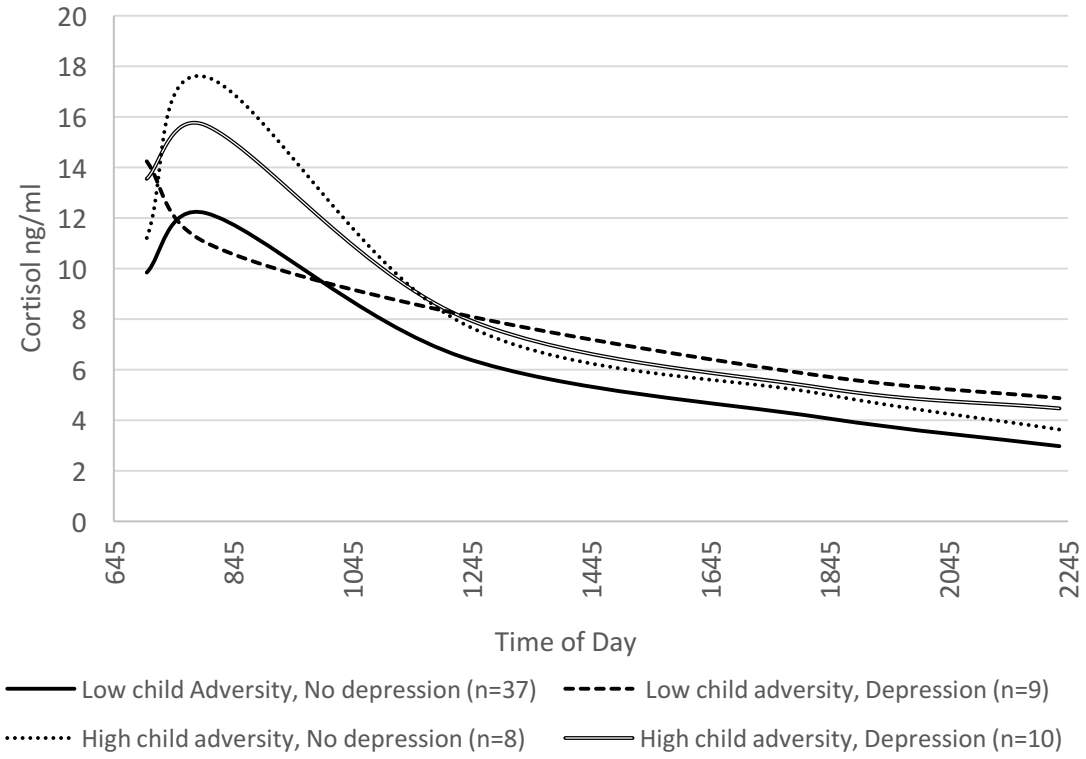

Figure 12. Childhood adversity and depression.
Line graph comparing diurnal cortisol trajectory between women with high and low childhood adversity and depression or no depression. There are distinct patterns for each sub-group of women.

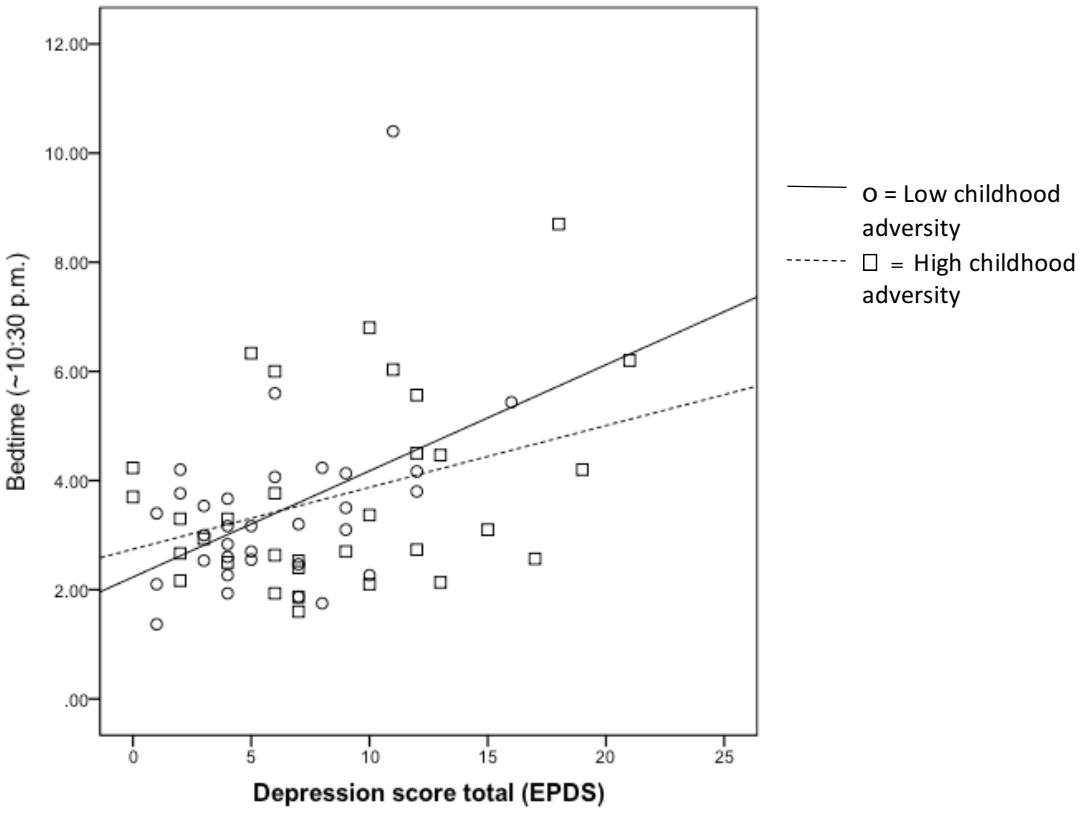

Figure 13. Depression and bedtime cortisol: Scatterplot of the interaction between depression (EPDS) and bedtime cortisol.
Women with high childhood adversity have dampened bedtime cortisol as depression score increases. The lines are comparing women with low and high childhood adversity.

A visual inspection of Figure 12 shows that there are also differences in the CAR among the four groups of women. Although there was no significant interaction, the CAR was plotted on a scatterplot (Figure 14) with prenatal depression and childhood adversity. There are two patterns that are evident from this graph. Women with depression appear to have a lower CAR, and as childhood adversity increases, CAR increases at a similar rate (parallel lines) for depressed and non-depressed women. To determine the amount of variability in the CAR that is explained by adult stress, childhood adversity and depression, we performed a step-wise linear regression, controlling for age and smoking, on the CAR. Depression significantly predicted a smaller CAR ($\beta = -.42$, $p < .01$) and childhood adversity significantly predicted a larger CAR ($\beta = .31$, $p < .01$). The model explained 21.6% of the variance of CAR ($R^2 = .216$, $F(2, 61) = 8.43$, $p < .01$).

Figure 15 shows in bar graph form that as depression scores increased, the CAR becomes smaller. In women with no depression (score 0 to 5), the CAR is 3 ng/ml, while the CAR for women with scores 10 or greater is less than 1, on average a three-fold difference. In Figure 16, childhood adversity scores are graphed with the CAR, demonstrating a U-shaped pattern.

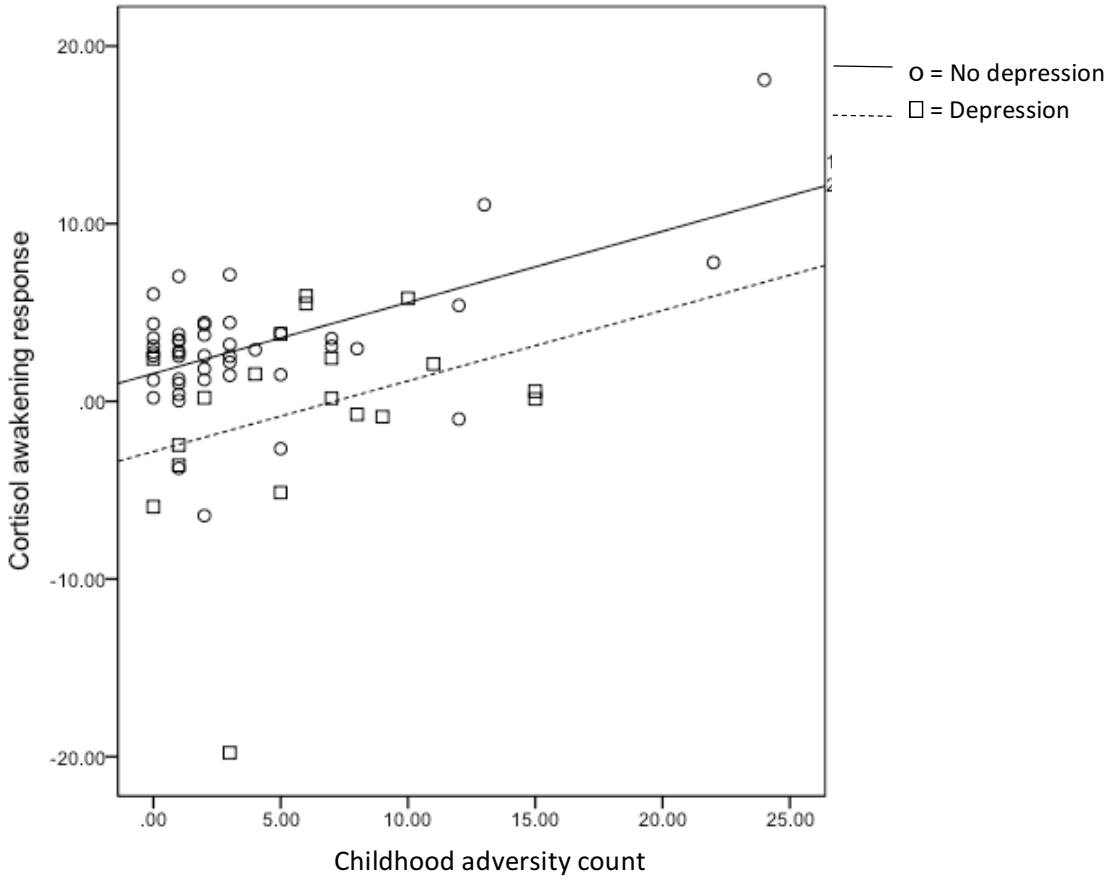

Figure 14. Childhood adversity and CAR: Scatterplot of the interaction between childhood adversity and the CAR.
Lines represent women with depression and no depression. CAR increases with higher childhood adversity but decreases with depression.

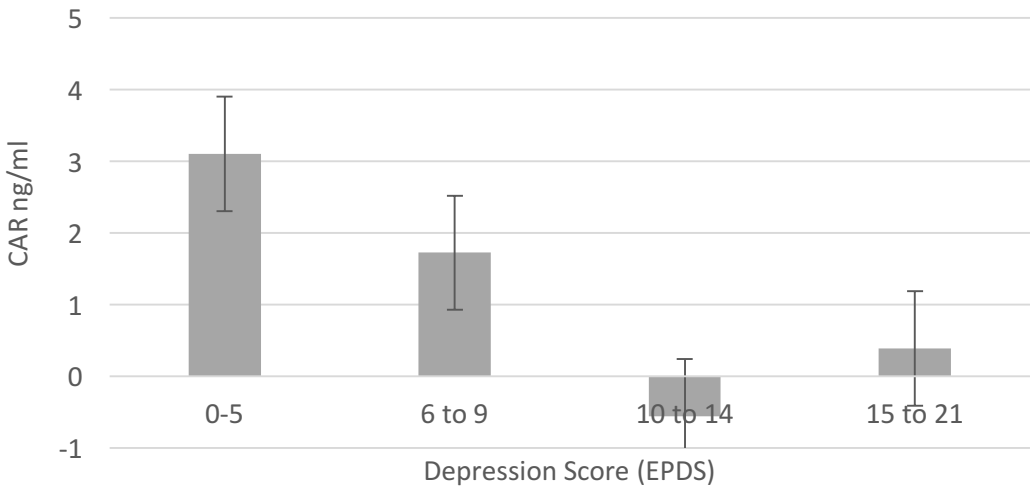

Figure 15. Depression and CAR: Bar graph of the CAR with increasing depression score. As depression scores increase, CAR decreases. Grouped by clinically relevant depression score intervals.

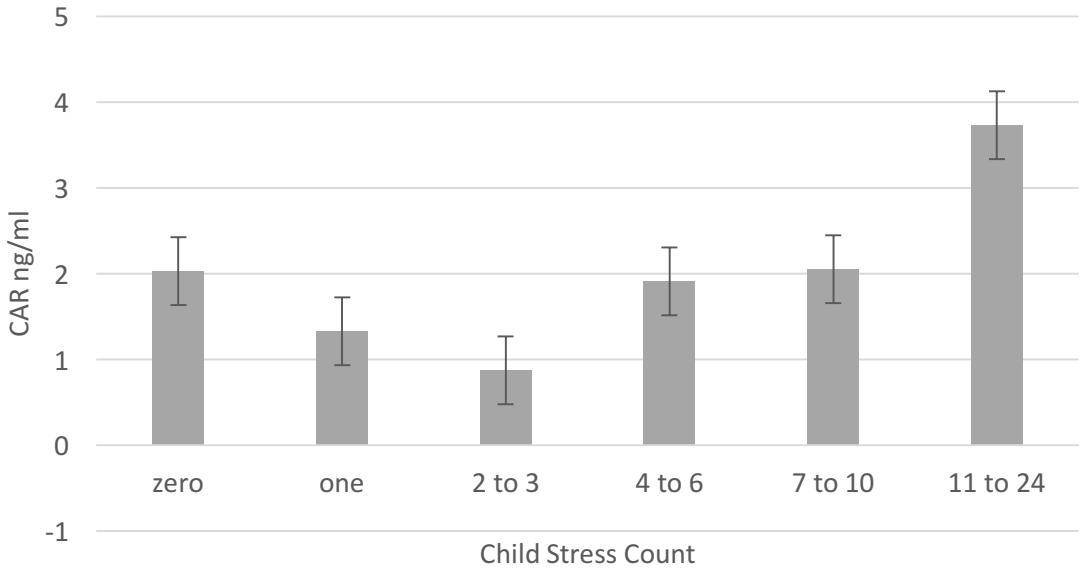

Figure 16. CAR by childhood adversity score categories.

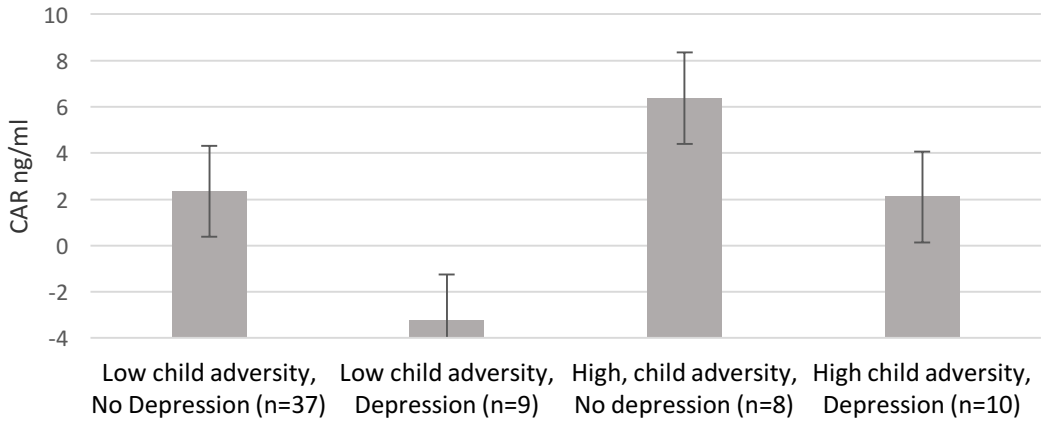

Figure 17. Depression X childhood adversity: Bar graph comparing the cortisol awakening response (CAR).
Four sub-groups of women categorized by prenatal depression and history of childhood adversity. Women with low child adversity and no prenatal depression (far left bar) have almost an identical CAR to the group of women with high childhood adversity and prenatal depression (far right bar).

Adult Stress Moderates Association between Depression and Cortisol

Adult stress and prenatal depression were highly correlated in Pearson correlations ($\rho = .46$ $p<.001$), so the next step was to differentiate prenatal depression and adult stress in their associations to cortisol. Using GLM, controlling for age, smoking and adult stress, depression predicted higher awakening cortisol, $F(4,59) = 11.51$, $p<.01$, $\eta = .16$ and smaller CAR, $F(4,59) = 10.9$, $p<.01$, $\eta = .156$. Adult stress was not associated with any of the cortisol parameters while controlling for prenatal depression. There was no significant interaction between adult stress and depression. Figure 18 demonstrates these findings a line graph. In an independent t-test comparing mean cortisol in only women with depression, those with high adult stress had significantly higher cortisol in the evening ($M = 6.50$, $SD = 2.7$, $t(17) = -2.25$, $p = .04$) and [marginally] at bedtime ($M = 5.39$, $SD = 2.51$, $t(17) = -1.76$, $p = .07$) compared to women with low adult stress (evening: $M = 4.15$, $SD = 1.31$; bedtime: $M = 3.56$, $SD = 1.45$). The mean AUCg was also significantly higher in depressed women with high stress ($M = 7945$, $SD = 2392$), compared to depressed women with low stress ($M = 5700$, $SD = 1311$, $t(17) = -2.6$, $p = .02$) There were no significant mean differences between high and low adult stress among women without prenatal depression.

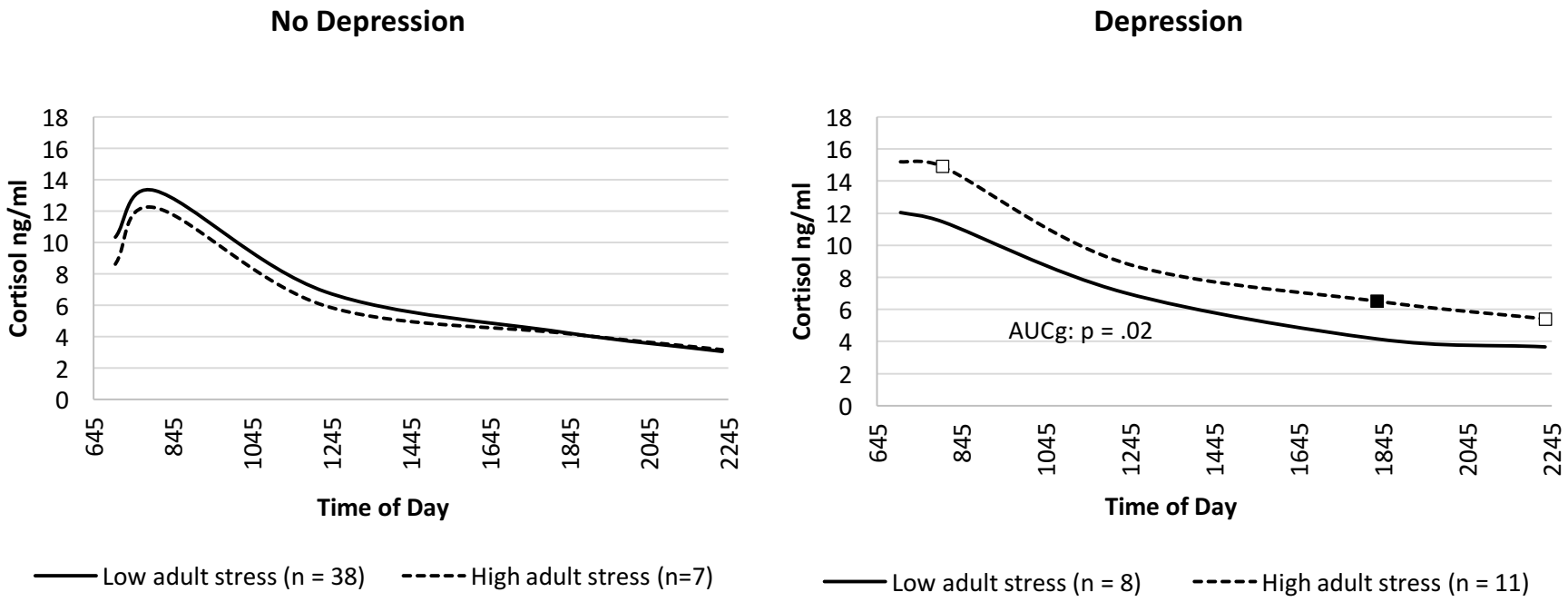

Figure 18. Depression X adult stress.
Line graphs comparing diurnal cortisol trajectory between women with and without depression.
Lines representing high and low adult stress. In non-depressed women, adult stress is not associated with higher cortisol, while in depressed women, higher adult stress is associated with higher cortisol over the course of the day. □ $p < .10$; ■ GLM $p \leq .05$

Duration, Domain, and Characteristic of Stress

Cortisol was associated with both acute and chronic domains of stress (see correlation tables in Appendix G). Lifetime acute stress events were associated with higher levels of evening ($r = .28$, $p < .05$) and bedtime cortisol ($r = .36$, $p < .05$) and greater total AUCg ($r = .26$, $p < .05$). When the number of acute life events are restricted to childhood, the count of acute life events is associated with higher cortisol at each time point (awake: $r = .29$; awake +30 $r = .44$, afternoon: $r = .25$; evening $r = .27$; bedtime $r = .25$, all $p < .05$). Chronic stress was only associated with higher morning cortisol (Awake + 30: $r = .28$, $p < .05$). The only domain of stress that was associated with higher morning cortisol was treatment / health stressors (Awake +30: $r = .36$, $p < .05$). Housing, financial stress, and life-threatening situations were associated with higher p.m. cortisol levels (range of r .25 - .37, $p < .05$). Reproductive-related stress was associated with lower (rather than higher) cortisol in the afternoon ($r = -.31$, $p < .05$) evening ($r = -.25$, $p < .05$) and at bedtime ($r = -.22$, $p < .05$). In terms of domains of stress, cortisol at bedtime was associated with physical danger ($r = .31$, $p < .05$) and humiliation ($r = .25$, $p < .05$). Cortisol was associated with role change/ reversal at awake + 30 ($r = .31$, $p < .05$) and in the evening ($r = .26$, $p < .05$).

Coping as a Moderator of Stress

Coping and health behaviors. Adult stress was significantly correlated with any smoking during pregnancy ($\rho = .35$, $p < .01$) and to an even greater degree with continued smoking during pregnancy ($\rho = .51$, $p < .01$). Adult stress was also correlated with poor health practices during pregnancy ($r = -.39$, $p < .01$). In a GLM analysis, the interactions between each of the 14 coping sub-scales with each of the stress variables were tested. No significant interactions were found in relation to health behaviors as measured by the HPQ-II. No further analyses were conducted for health behaviors as the outcome.

Cortisol: Main effects of coping

Main effects of coping. Prior to testing for interactions, main effects for each of the 14 sub-scales were tested in multivariate GLM including all cortisol parameters as the outcome. Only the sub-scale of seeking emotional support was significant for a main effect on cortisol. Women who reported seeking more emotional support from others had lower cortisol in the afternoon ($F(1,65) = 4.30$, $p=.04$, $\eta = .062$), evening ($F(1,65) = 6.27$, $p=.02$, $\eta = .088$), and at bedtime ($F(1,65) = 4.12$, $p=.05$, $\eta = .06$). Seeking emotional support also predicted lower total daily cortisol (AUCg: $F(1,65) = 3.57$, $p=.063$, $\eta = .052$).

The two subscales of seeking emotional support and seeking instrumental support followed the same interactional pattern in later analyses, and are theoretically similar in that they are the only two scales on the Brief COPE which assess an individual's willingness to seek support from other people. Therefore these sub-scales were summed to create a "seeking support" scale, thereby increasing the variability in the seeking support construct.

Coping sub-scales and cortisol. In GLM analyses testing the interaction between coping and stress, 29 individual interactions were significant on the cortisol outcomes. The majority of the significant interactions involved the stress sub-categories of childhood adversity and prenatal depression. For the interaction between coping sub-scales and childhood adversity, the interactional pattern was the same across all coping subscales when plotted into scatterplots. The observed pattern from the scatterplots was that for women with high childhood adversity, use of more coping was associated with lower cortisol levels, while for women without childhood adversity, use of coping was not associated with any change in cortisol.

Because there were no apparent differences in the direction or pattern of interactions within the coping sub-scales, all 14 sub-scales were summed to create a total Brief COPE score.

This total score was then tested in GLM in an interaction with childhood adversity, controlling for age and smoking. The total COPE interacted significantly with childhood adversity (dichotomous variable) on AUCg, $F(5,58) = 5.33$, $p=.03$, $\eta = .084$ and marginally for Awake +30, $F(5,58) = 3.67$, $p = .06$, $\eta = .060$.

In the GLM analyses examining the interaction between coping and childhood adversity, both variables are entered as continuous variables. In this case, either variable can be considered the moderator. In order to interpret the interaction identified here, two interaction plots were constructed with 1) coping as the moderator (in line with original study conceptual model and hypothesis), and 2) childhood adversity as the moderator. While the statistical interaction is identical either way, the interpretation differs based on which variable is declared as the moderator. If coping is declared as the moderator (option 1), the interpretation would be as follows: Among women using less coping strategies, childhood stress has no association with cortisol, whereas among women using more coping strategies, childhood stress is associated with higher cortisol (see scatterplot in Figure 19). If childhood adversity is declared as the moderator (option 2), the interpretation would be as follows: Among women with higher childhood stress, use of more coping is associated with a greater reduction of cortisol, whereas among women with lower childhood stress, use of more coping is associated with no change in cortisol (see scatterplot in Figure 19).

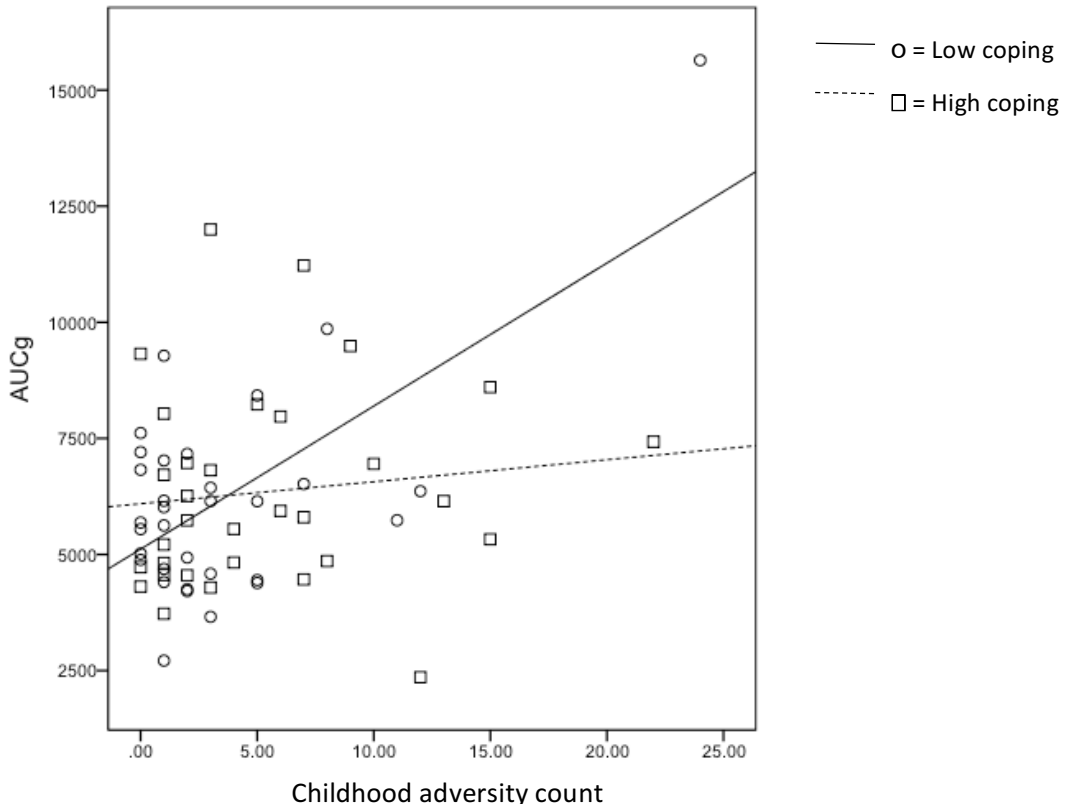

Figure 19. Childhood adversity X coping: Scatterplot on AUCg.
Among women using less coping strategies, childhood stress had no association with cortisol AUCg. Among women using more coping strategies, childhood stress is associated with higher cortisol AUCg. Split file correlations: Low coping: r=.30, p=.10; High coping: r=.10, p=.59. High and low coping groups were cut at the median COPE score. Interaction term (childhood adversity X coping): F (5,58) = 5.33, p=.03, η = .084.

Childhood adversity was selected as the moderator (a revision to the original hypothesis) because the interpretation associated with option 2 (Figure 20) made more theoretical sense. Although usually the moderator is chosen based on which variable comes first in time, here the childhood adversity score is considered a proxy for current dysregulation of the HPA system in pregnancy. For these reasons, the remainder of the interaction analyses considered the stress subscales as the moderator of coping.

The interaction between coping and childhood adversity on the awake + 30 minutes time is shown in Figure 21. The interaction term was marginally significant, $F(5,58) = 3.67$, $p = .06$, $\eta = .060$. Data were then dichotomized into high and low childhood adversity and correlated separately with cortisol. In women with high childhood adversity, cortisol and coping were highly correlated. In women with high childhood adversity, use of more coping was associated with lower cortisol levels at awake +30 minutes ($r = -.57$, $p=.01$), whereas women with low childhood adversity showed no correlation ($r = .11$, $p = .48$).

Coping and depression. The total coping score also interacted with prenatal depression on afternoon cortisol (Figure 22), $F(5,60) = 5.50$, $p = .02$, $\eta = .084$ and on evening cortisol. The correlation between coping and afternoon cortisol was positive ($r=.32$, $p=.16$) for women with depression, while the relationship was negative ($r=-.31$, $p=.04$) for women without depression. The sub-scales that interacted significantly include distraction, active coping and positive reframing.

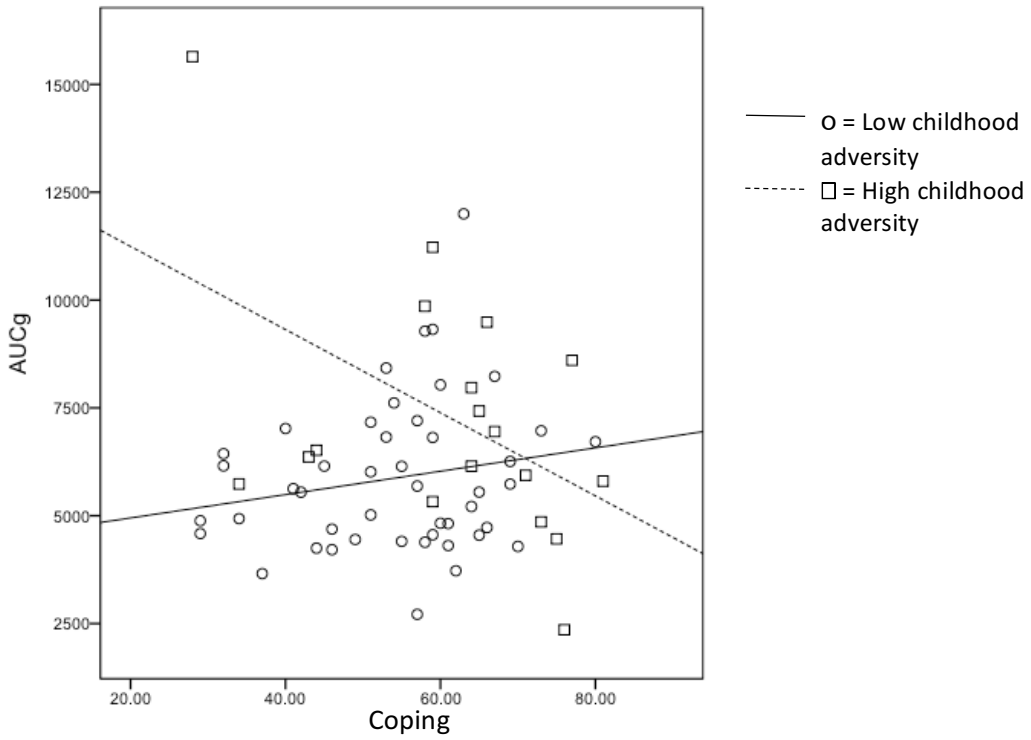

Figure 20. Coping X childhood adversity: Scatterplot of interaction on AUCg.
Among women with higher childhood stress, use of more coping is associated with a greater reduction of cortisol AUCg. Among women with lower childhood stress, use of more coping is associated with the same or higher cortisol AUCg. Dichotomous data correlations: high stress: r=-.40, p=.10 (n=18); low stress: r=.19, p=.21 (n=46). High and low coping groups were cut at the median COPE score. Interaction term (coping X childhood adversity): F (5,58) = 5.33, p=.03, η = .084.

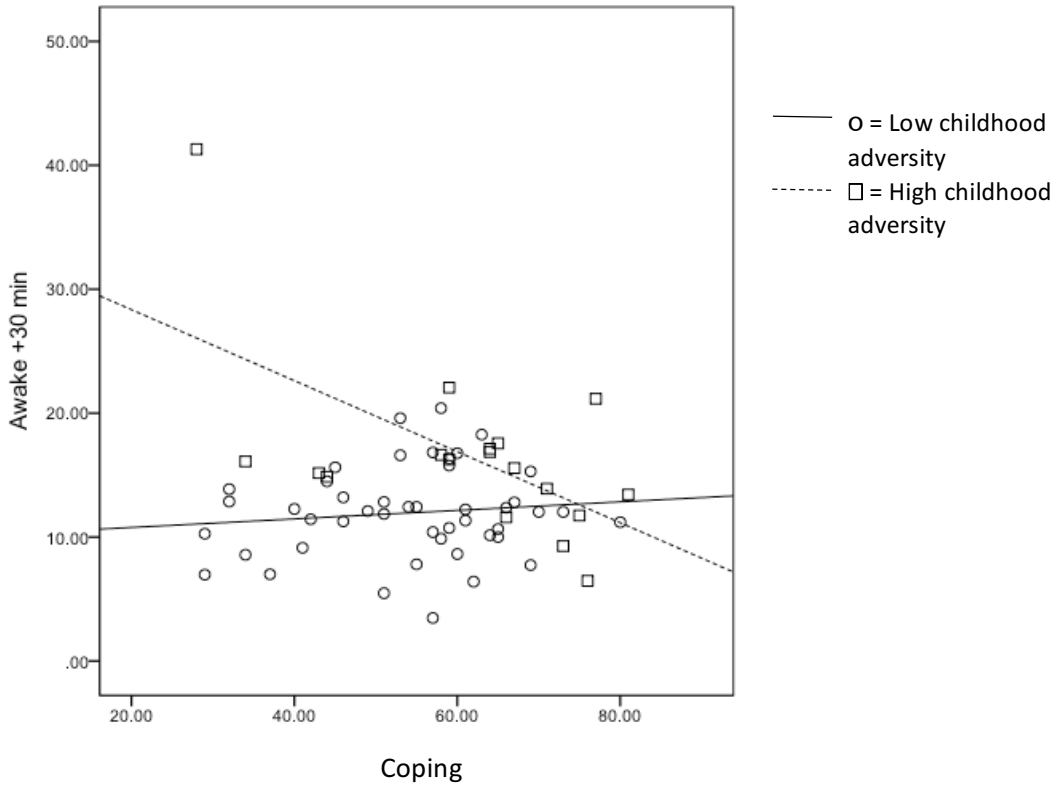

Figure 21. Coping X childhood adversity Scatterplot of interaction on awake +30 minutes. Split correlations: High child adversity: R=-.57, p=.01; Low child adversity: r = .11, p = .48. Interaction term (coping X childhood adversity): F(5,58) = 3.67, p = .06, η = .060.

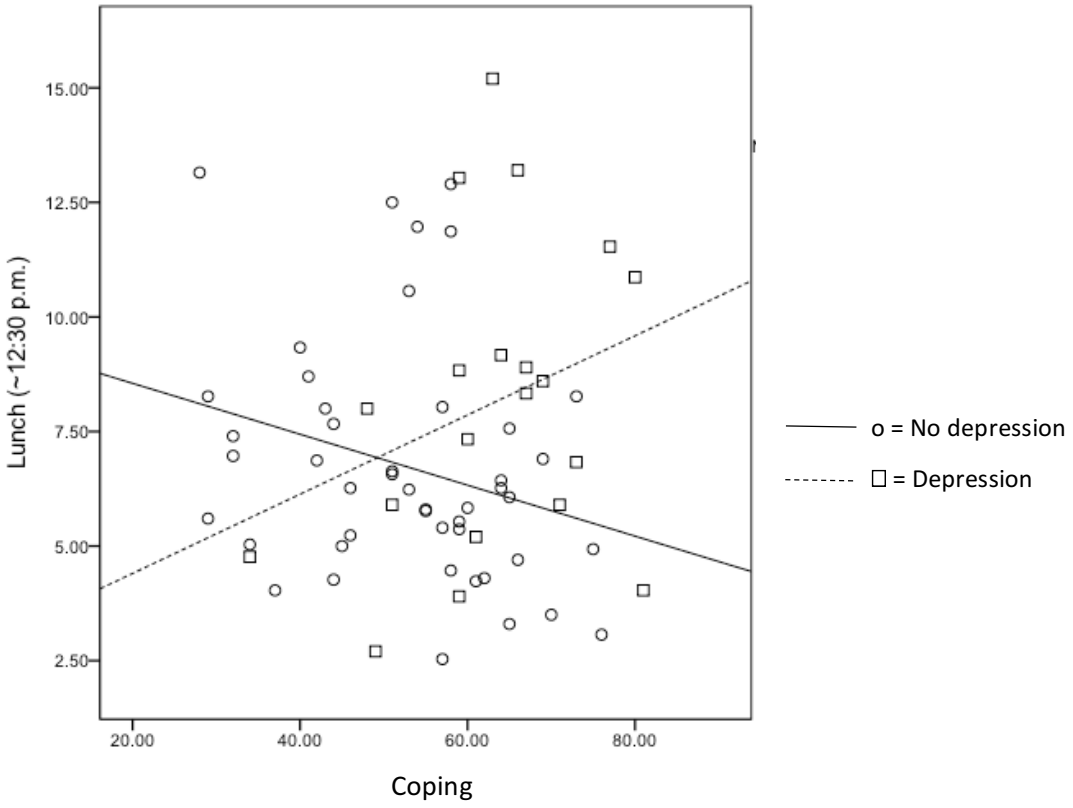

Figure 22. Coping X prenatal depression: Scatterplot of interaction on afternoon cortisol. Split correlations: No depression: r=-.31, p=.04; MDD: r=.32, p=.16. Interaction term (coping x prenatal depression): $F(5,60) = 5.50$, $p = .02$, $\eta = .084$.

Role of Seeking Support in attenuating HPA response

Using GLM controlling for age and smoking, the interaction between each stress variable (childhood adversity, adult stress, prenatal depression) was tested for an interaction with support seeking on all cortisol parameters. There were no significant interactions between support seeking and childhood adversity on cortisol, although there was a significant interaction for adult stress (controlling for age, smoking and depression) on bedtime cortisol (Figure 23) $F(6,57) = 9.57$, $p < .01$, $\eta = .144$ and diurnal slope, $F(6, 57) = 6.08$, $p = .02$, $\eta = .096$. There was also a significant interaction for depression (controlling for age, smoking, and adult stress) and support seeking on bedtime cortisol (Figure 24), $F(6,57) = 3.93$, $p = .052$, $\eta = .065$) and CAR (Figure 25), $F(6,57) = 4.04$, $p = .049$, $\eta = .066$. When data were dichotomized by depression score, the correlation between support seeking and bedtime cortisol was significant (ρ=-.47, p=.04) only for the subset of women with prenatal depression. The interaction plot (Figure 24) shows that for women with prenatal depression, as support seeking increases, CAR tends to increase as well (though not significantly correlated when split: ρ =.12, p=.63).

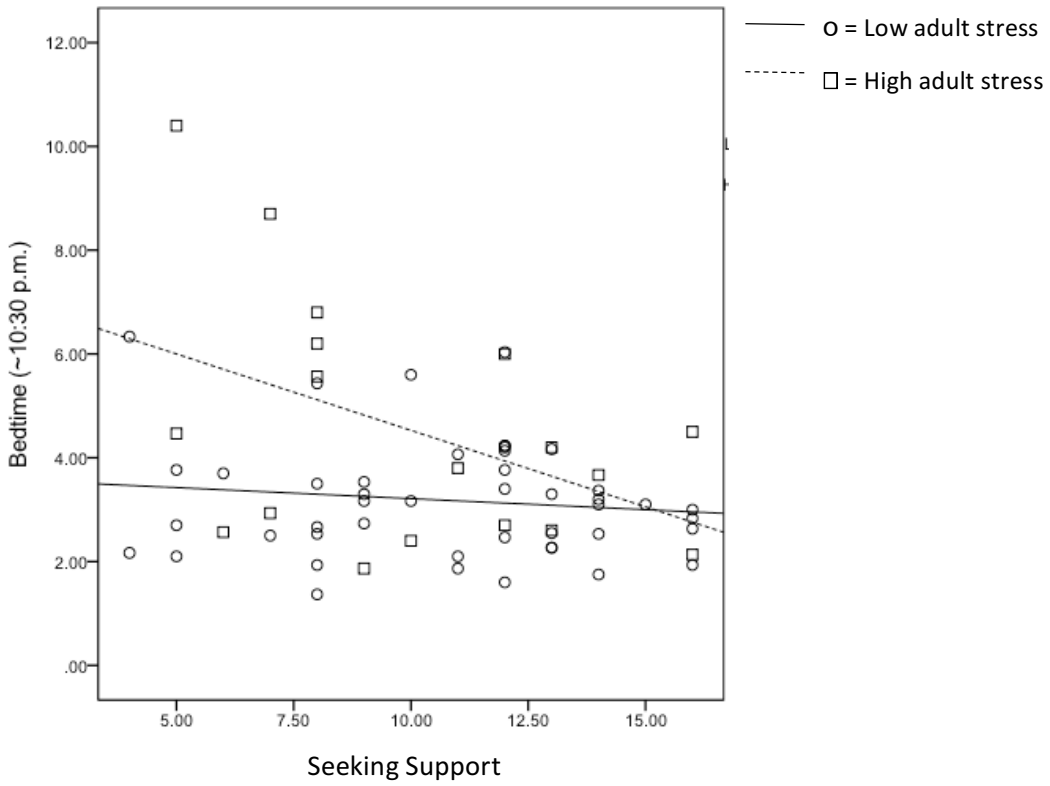

Figure 23. Seeking support X adult stress: Scatterplot of interaction on bedtime cortisol. Split correlation: High adult stress: ρ =-.36, p=.14; Low adult stress: ρ = -.08, p= .62. Interaction term: F(6,57) = 9.57, p < .01, η = .144

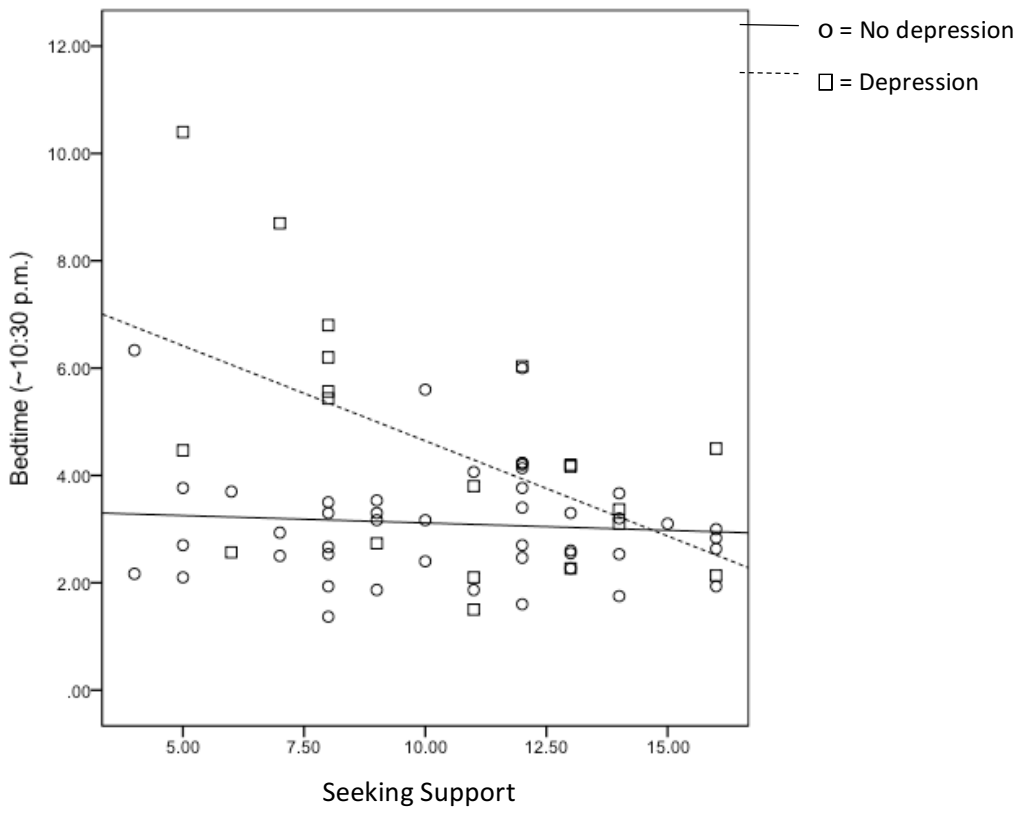

Figure 24. Seeking support X prenatal depression: Scatterplot of interaction on bedtime cortisol. Split correlation: Depression: ρ=-.47, p=.04, No depression: ρ = -.03, p = .83.

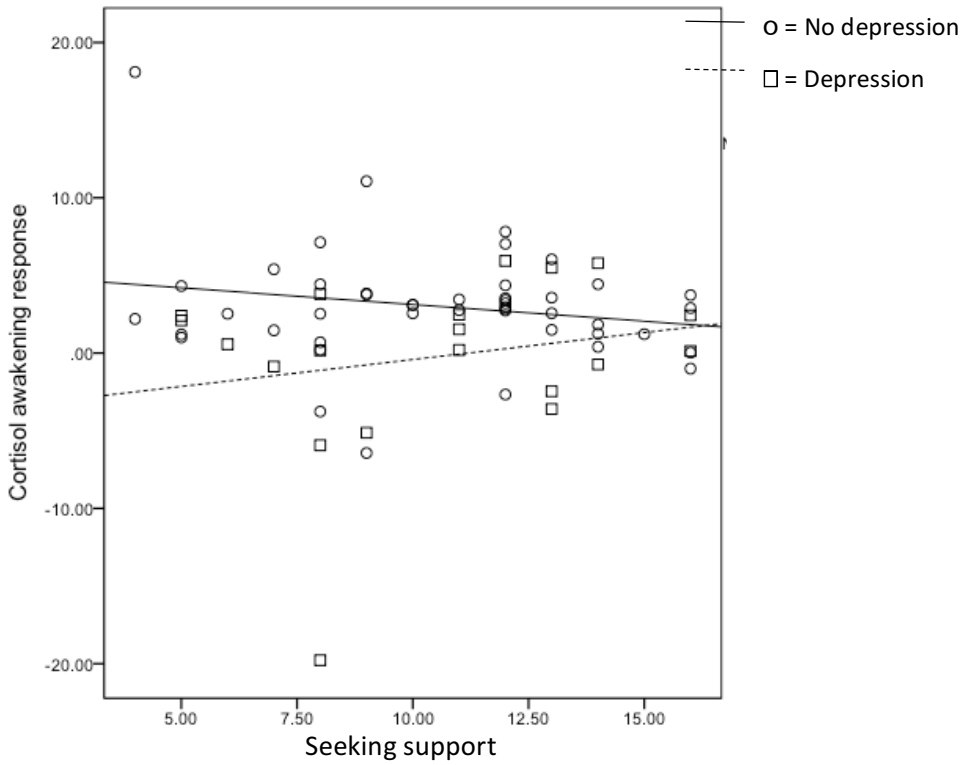

Figure 25. Seeking support X prenatal depression: Scatterplot of interaction on CAR. Split correlations: n.s. ρ =.12, p=.63; Interaction term: F(6,57) = 4.04, p = .049, η = .066.

Birth Outcomes

In GLM analysis controlling for age, smoking and race, seeking support interacted with childhood adversity at a marginally significant level to predict length of gestation $F(5,55) = 3.49$, $p = .067$, $\eta = .06$. Upon examining the interaction in a scatterplot, it was apparent that one outlier was skewing the data to produce the interaction. The case involved a sudden pregnancy complication at 34 weeks gestation followed by fetal demise. A bar graph including all cases is shown in Figure 26, and the same graph is shown in Figure 27 with the one outlier case removed. In GLM with the outlier case removed, the interaction no longer predicted length of gestation. However, in looking at the bar graph in Figure 27, the groups with high support seeking show a pattern for longer gestation in both high and low adversity groups, although there was not a significant correlation ($\rho = .094$, $p = .454$). When means were compared between the two groups in an independent t-test, there was no statistically significant difference (low support seeking: $M = 275.8$ days, $SD = 8.4$; high support seeking: $M = 277.3$ days, $SD = 10.5$, $t(63) = -.638$, $p = .526$). However, the pattern was explored further given the prior analyses indicating that support seeking was associated with reduced cortisol in the evening and increased CAR for depressed women.

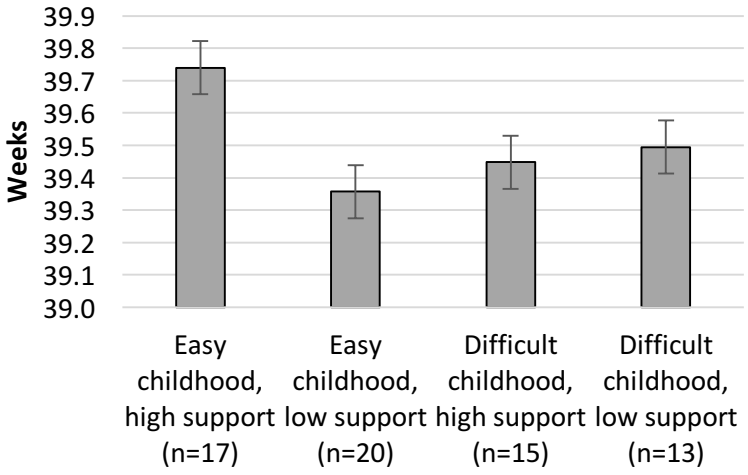

Figure 26. Length of gestation: sub-groups based on high/low childhood adversity and high/low support seeking.
All cases included. Error bars = 1 standard error.

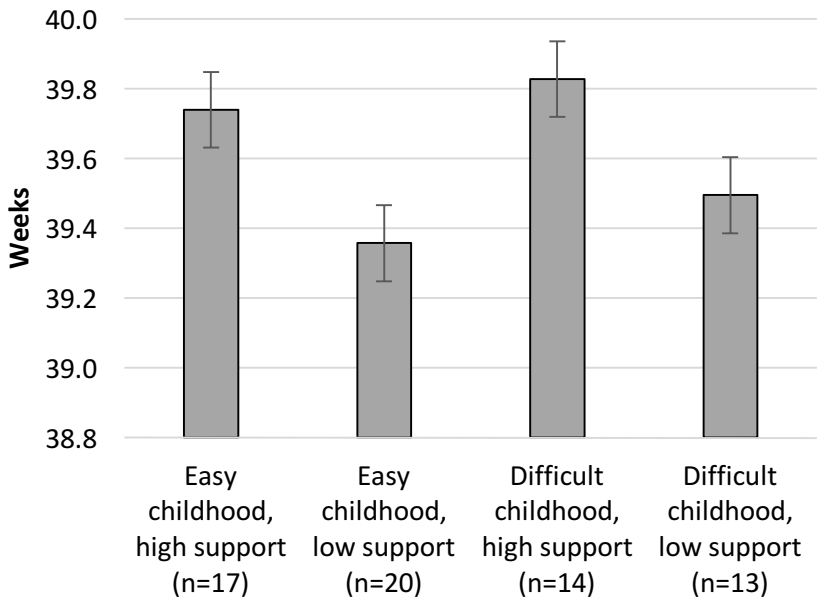

Figure 27. Length of gestation: sub-groups based on high/low childhood adversity and high/low support seeking.
Support seeking appears to lengthen gestation in both groups of childhood adversity. One outlier excluded. Error bars = 1 standard error.

The relationship between support seeking and cortisol trajectory was examined in women with high childhood adversity, and compared to women with low child adversity (both high and low support seeking) (Figure 28). In an independent t-test, the awake +30 minute cortisol did not differ within the high childhood adversity group between high and low support seeking ($t(16) = 1.59$, $p = .13$). However, women with high childhood adversity and low support seeking differed significantly from women in the low childhood adversity group ($t(32) = -3.27$, $p = .008$).

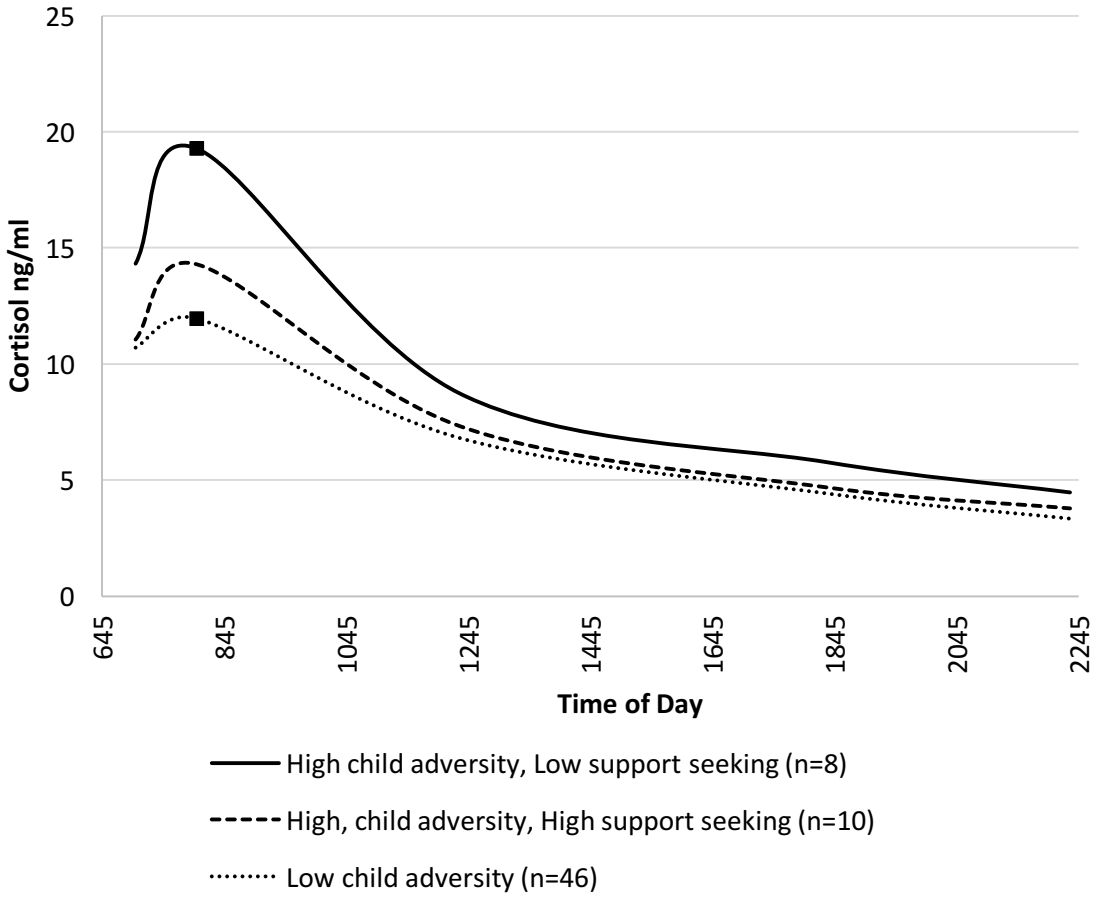

Figure 28. Childhood adversity X support seeking: Comparison of diurnal cortisol trajectory for women with high childhood adversity.
Low childhood adversity (both high and low support seeking) is the reference group. At awake + 30, high child adversity and low support seeking was significantly different from the reference group, but high child adversity, high support seeking was not significantly different from the reference group. ■ p = .001 in relation to reference group (low child adversity).

The relationship between support seeking and diurnal cortisol trajectory was examined in Figure 29, which shows a pattern for a graded response to support seeking in women with high childhood adversity. There is a pattern for support seeking to attenuate cortisol levels in high childhood adversity towards levels comparable to low childhood adversity. However, the sample sizes are small, and no significant differences were found. This pattern of graded response is also evident in the slope (Figure 30) and AUCg (Figure 31).

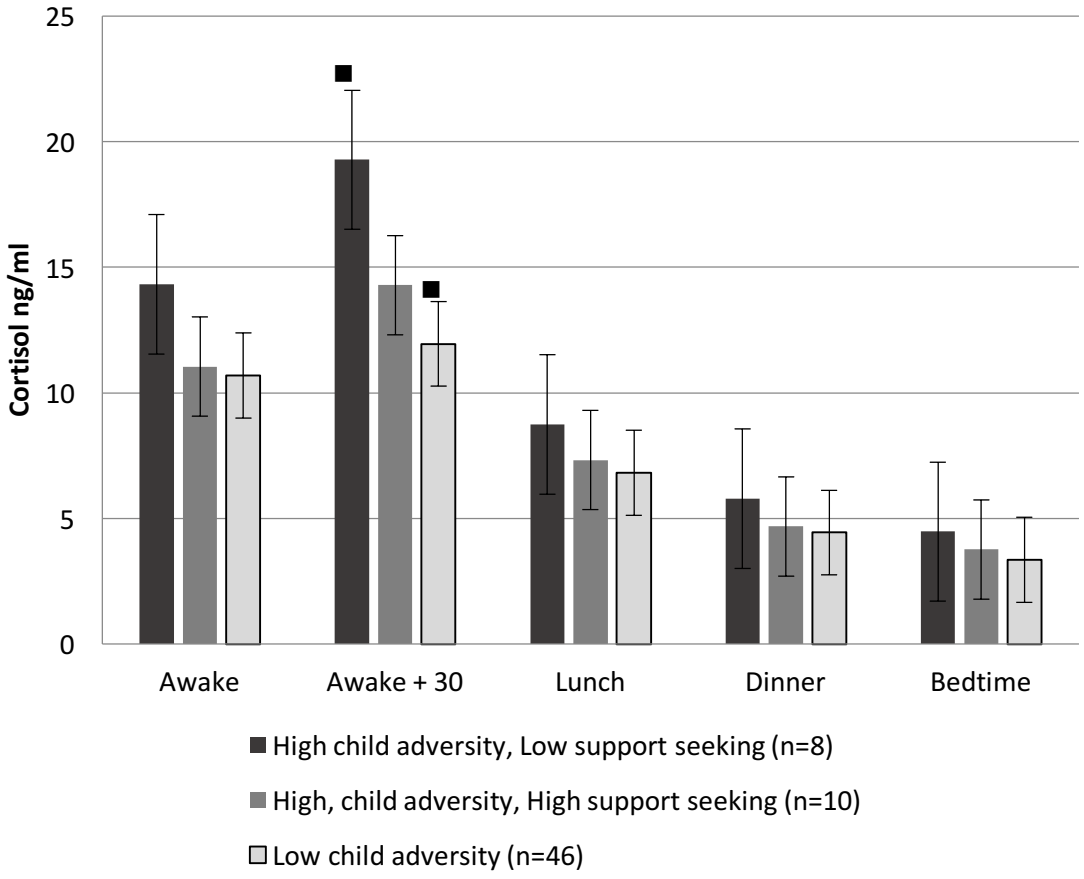

Figure 29. Childhood adversity X support seeking: Bar graph of diurnal cortisol trajectory across 3 groups.
The low adversity group is considered the reference group. There is a pattern for graded response. ■ p = .001.

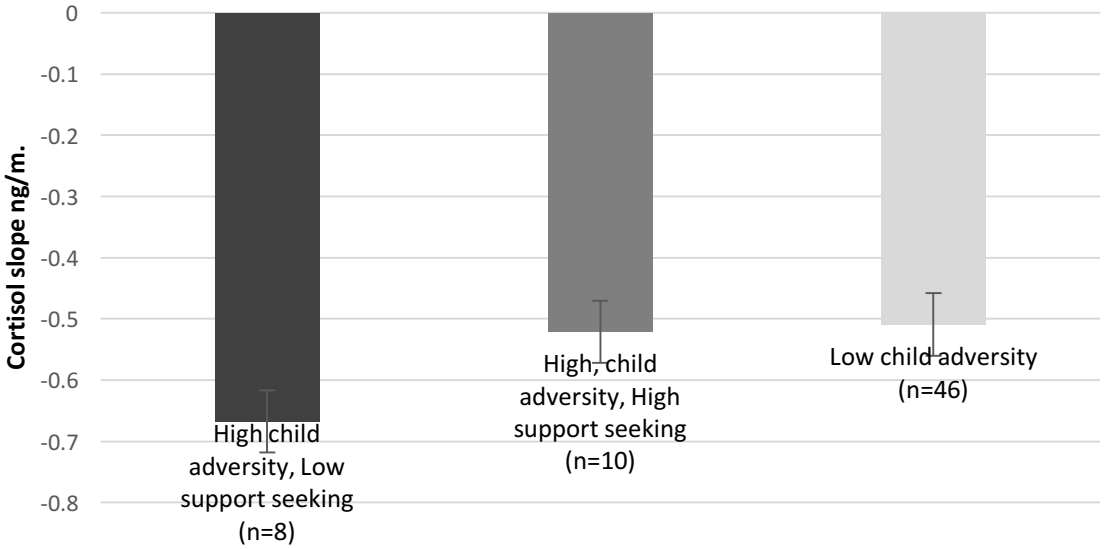

Figure 30. Diurnal slope for groups based on childhood adversity and high or low support seeking.
There is a pattern for graded response, though no significant differences.

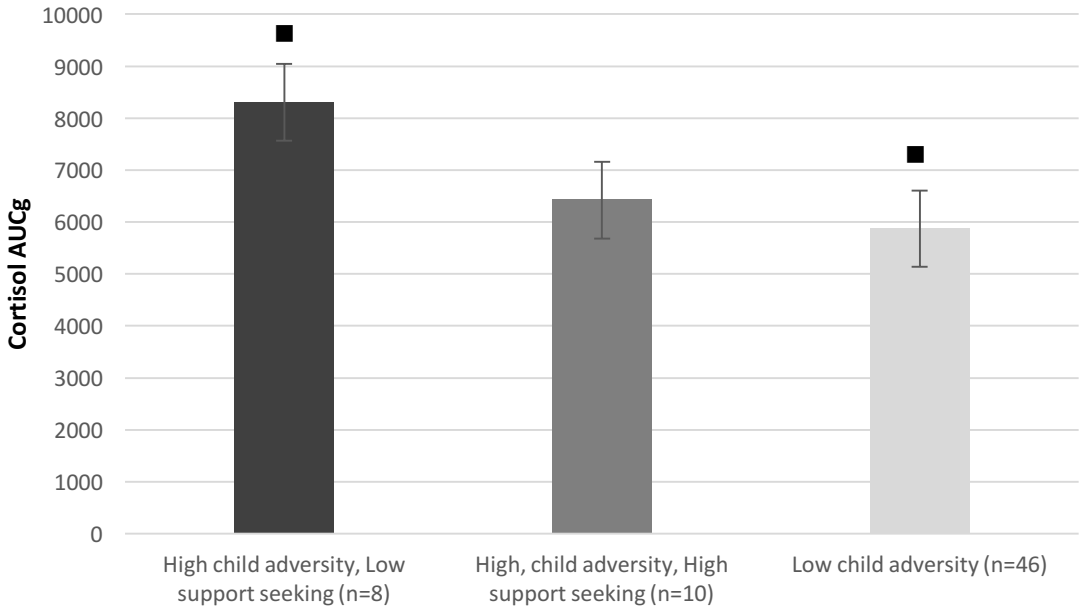

Figure 31. AUCg for groups based on childhood adversity and high or low support seeking. There is a pattern for graded response. ■ p = .02.

The relationship between prenatal depression and support seeking was also examined in relation to cortisol. Figure 32 shows the diurnal cortisol trajectory for women with 1) no depression, 2) depression and high support seeking, and 3) depression and low support seeking. The graph shows a pattern for attenuation of cortisol in the evening associated with high support seeking, as well as a normalization or restoration of the CAR in depression towards what is seen in non-depressed women. There is also a pattern of graded response in the CAR (Figure 33) and AUCg (Figure 34) for depressed women with high support seeking towards levels comparable to non-depressed women.

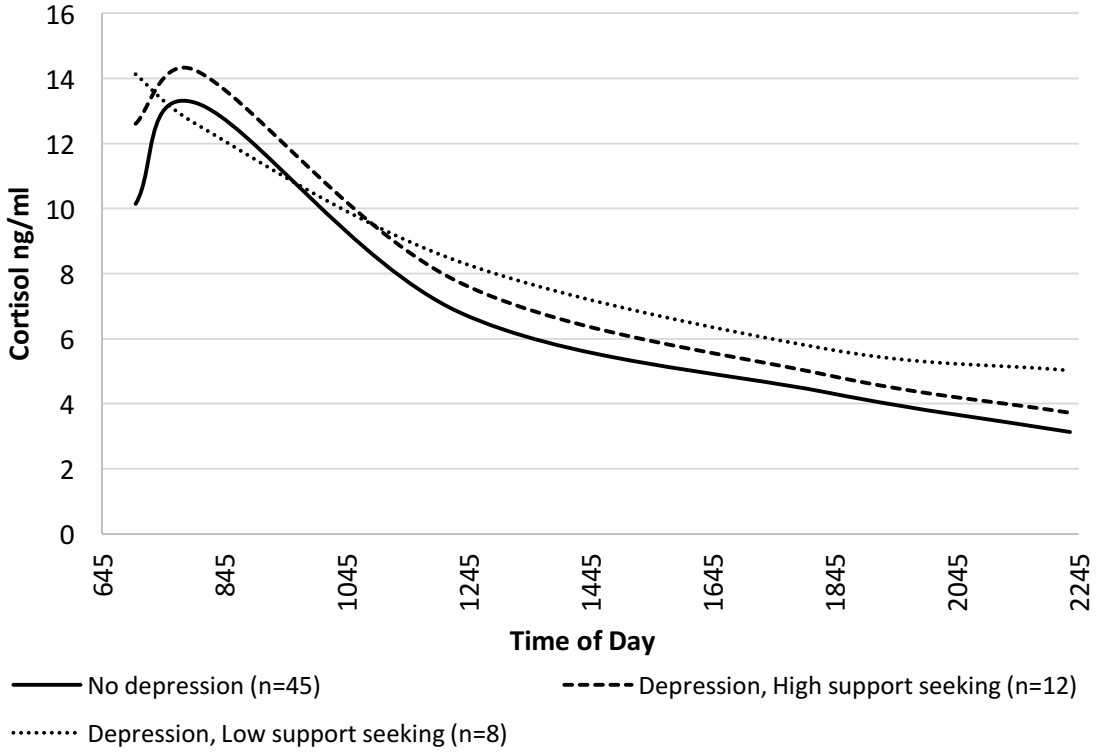

Figure 32. Prenatal depression and support seeking on diurnal cortisol trajectory. High support seeking appears to restore / maintain CAR in prenatal depression. ■ $p < .05$ in relation to reference group (low child adversity); awake: $p = .048$; bedtime: $p = .004$

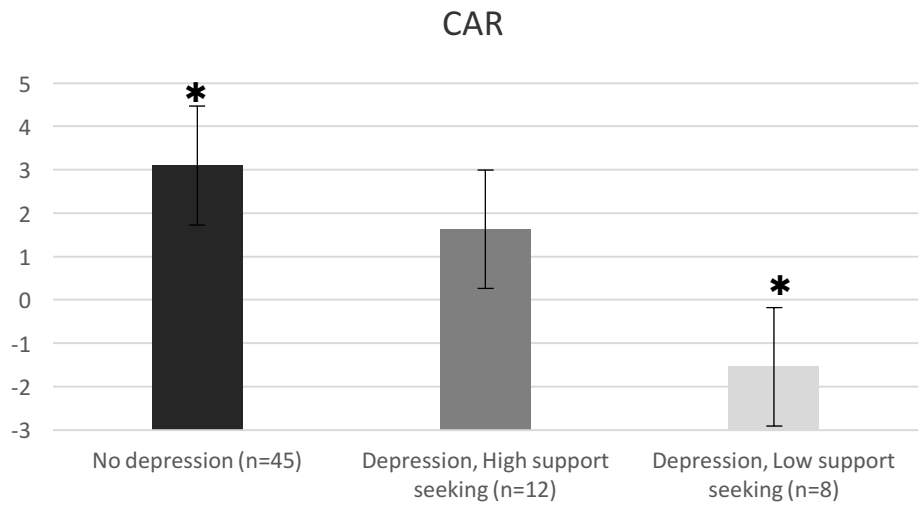

Figure 33. Prenatal depression and support seeking on CAR.
There is a pattern for graded response. ✱ p = .002.

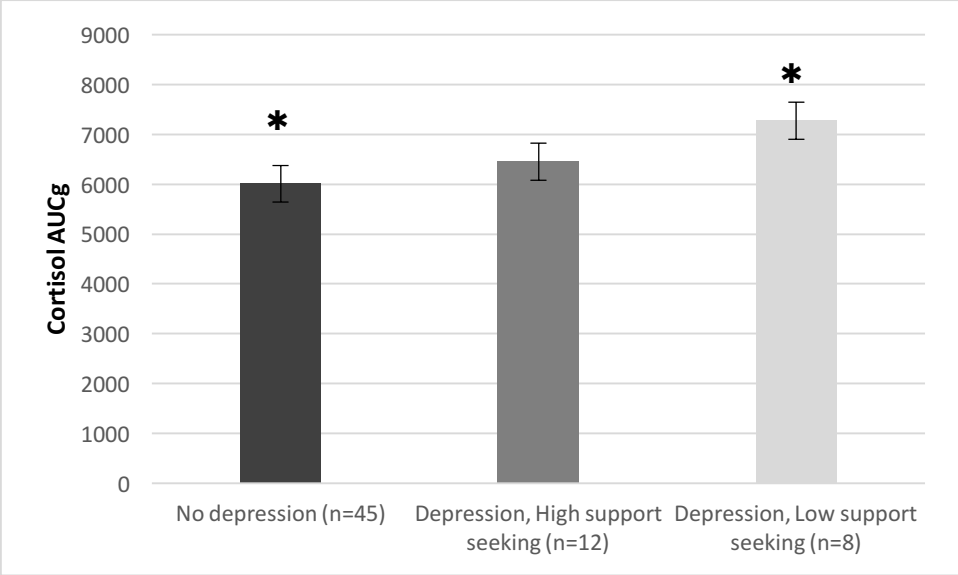

Figure 34. AUCg by depression and high or low support seeking.
There is a pattern for graded response. ✱ p = .04.

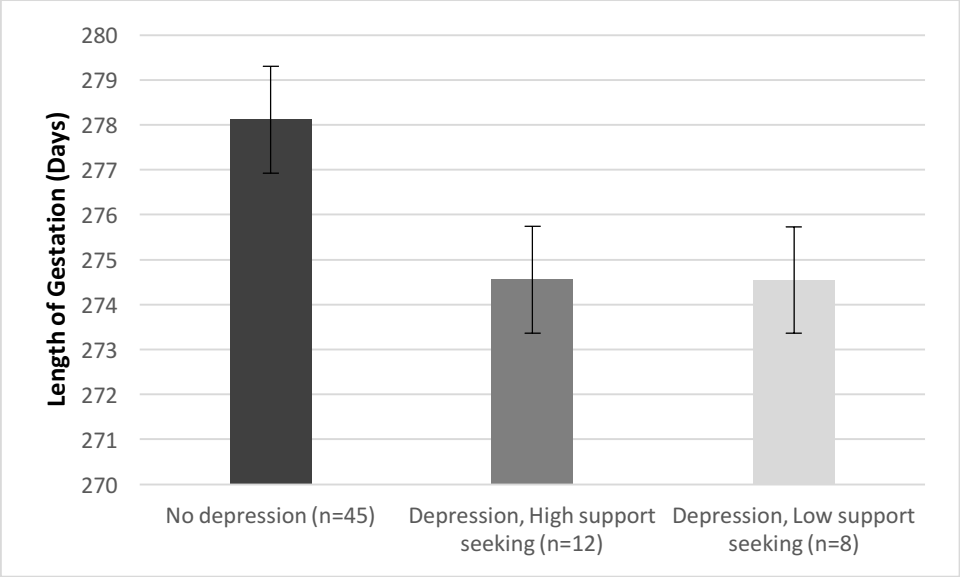

Figure 35. Length of gestation by depression and high or low support seeking. Seeking support does not appear to have an association with length of gestation. Depressed women have a shorter gestation by 3.5 days, regardless of high or low support seeking. No significant differences in means between groups.

Although higher support seeking showed a pattern of attenuated cortisol in depressed women, length of gestation was not different among depressed women with high or low support seeking. Women with no depression showed a pattern of longer gestation, although there was not a statistically significant difference (Figure 34).

Another notable difference in birth outcomes between women with high and low lifetime stress was with rates of vaginal versus cesarean delivery. Women with high childhood adversity, were statistically more likely to have a Cesarean delivery, rather than vaginal delivery. High lifetime stress and adult stress were marginally associated with higher Cesarean delivery, while depression was not (Lifetime stress: $\chi = 3.22$, $p = .07$; Adult stress: $\chi = 3.22$, $p = .07$; Child adversity: $\chi = 10.27$, $p = .001$; Depression $\chi = .03$, $p = .86$).

Discussion

Overall this study found that total lifetime stress was associated with higher cortisol levels in pregnant women in the morning and evening, as well as total daily cortisol exposure. Childhood adversity was positively associated with higher awakening, 30 minutes post-awakening and CAR. Higher morning cortisol was accounted for primarily by childhood adversity, while higher evening levels were accounted for primarily by stress and depression in adulthood. Adult stress only reached significance in an uncontrolled t-test and not GLM. These findings are in line with other recent studies. Gillespie et al. (2017) also used the STRAIN to examine the association between cortisol and childhood adversity / adult stress in pregnant women. This group similarly found that cortisol (collected in the early afternoon) was more strongly correlated with childhood adversity, but less so with adult stress. Longitudinal studies with pregnant women have found childhood adversity (i.e. sexual abuse) is associated with increasing CAR over pregnancy (Bublitz & Stroud, 2012), rather than the normal pattern of attenuated CAR as

pregnancy advances. Attenuation occurs in the second half of pregnancy, so the findings of our study may have demonstrated this same lack of attenuation. Since our study was not longitudinal, attenuation could not be examined directly.

Other studies have found childhood trauma to be associated with lower baseline morning cortisol (Shea et al., 2007). This discrepancy could be related to differences in the population sample in terms of race and socioeconomic status, or could be related to differences in the analysis of childhood adversity as a continuous (Shea et al., 2007) versus categorical variable (e.g. Bublitz & Stroud, 2012). In a study of pregnant adolescents, abuse history was not associated with AUCg, although AUCg was associated with shortened gestation and lower birth weight. The reason for null findings in this study may likewise be associated with the analysis of childhood adversity on a continuous scale (rather than categorical).

In our analyses, we found that the use of a clinically meaningful cut-point made a difference in the effect size between cortisol and stress / adversity. The cut-point used was a 30:70 ratio, which was based on prior data suggesting that approximately 30% of women have experienced levels abuse and adversity severe enough to cause long-term psychological and physiologic adjustments (Records & Rice, 2009). We suggest that future studies consider the use of categorical, rather than continuous analysis of childhood adversity data.

This study also found that depression was associated with cortisol. Baseline morning cortisol was higher, resulting in a 3-fold smaller CAR. This finding is consistent with other studies in non-pregnant women (Stetler & Miller, 2005)**.** Although not all studies support this finding (Bublitz et al., 2016). Two explanations could account for this pattern. The first is that depressed women could have a true blunted response to morning awakening. The other explanation is that the cortisol awakening response could be occurring in depressed women slightly prior to awakening,

resulting in a measurement of the latter downward slope of the CAR, rather than the start of the CAR. This explanation is consistent with the phenomenon of early morning awakening as a symptom of depression (Sadock & Sadock, 2011), for which an advanced/precipitous CAR could be partly responsible. Prior studies have documented that depressed individuals show an earlier rise in night-time cortisol levels compared to non-depressed individuals (Halbreich, Asnis, Shindledecker, Zumoff, & Nathan, 1985). However, other authors (Stetler & Miller, 2005) have argued that depression causes a true blunting of the CAR, rather than a circadian phase-shift, explaining that phase shifts of the trough are not evident later in the day among depressed individuals. The role of circadian rhythms and sleep patterns in relation to cortisol in pregnancy is an area for further research.

We also found that interactions involving depression were significant only if depression was used as a dichotomous, rather than continuous variable, suggesting that the cut-off of 10 on the EPDS was a clinically meaningful cut-point. This is consistent with other studies measuring depression in pregnant women, finding that effect sizes for the relationship between depression and birth outcomes were larger when a dichotomous measure of depression was used in the analysis (Grote et al., 2010), compared to continuous. This is in line with the method of validation for most depression scales, including the EPDS, which is based on the gold-standard diagnostic interview for major depressive disorder, a dichotomous variable (depressed or not depressed). The measurement of depressive symptoms in women who do not meet cut-off for even minor depression is not likely to be valuable or meaningful data, and thus, dichotomous analyses of depressive symptoms are suggested. The inappropriate analysis of depression scales as continuous variables increases the risk of type II errors, thereby minimizing and delegitimizing the true adverse biological effects of depression. From a methodological standpoint, it is

important to use clinically meaningful cut-points when using stress and depression as variables in research.

Since childhood is a critical developmental period more sensitive to environmental programming influences on the HPA axis, we examined whether childhood adversity moderated the relationship between cortisol and adult stress or cortisol and depression. From an evolutionary perspective (Seckl, 2008), childhood adversity would prime the HPA system to effectively handle similar types and severities of adversities later in life. We found that exposure to childhood adversity significantly interacted with both adult stress and depression. Women who experienced the highest counts (i.e. upper 1/3) of childhood adversity did not show an elevated response to high adult stress or depression in the evening, whereas women without childhood adversity did show an elevated evening cortisol response. The same pattern was true for depression-related blunting of the CAR. Only women who did not experience high childhood adversity showed a blunted CAR, whereas women with high childhood adversity did not appear to be affected by the blunting effects of depression. These findings are in line with those of Bublitz et al. (2016) who found that women with a history of childhood sexual or physical abuse had attenuated response to momentary stressors. A somewhat contrary finding by the same group (Bublitz & Stroud, 2013) is that pregnant women with a history of childhood adversity (i.e. sexual abuse) showed increased morning cortisol related to prior day stress, and increased evening cortisol related to same-day stress. Together these findings suggest that women who experience high childhood adversity show a response that is at first blunted or delayed, but then prolonged. Our data add to this pattern, in that long-term alterations in cortisol set-points do not adjust to higher levels of stress or depression. The HPA systems of maltreated women may have lost to ability to respond to environmental stressors (i.e. differential susceptibility), or may be unable to mount an appropriate response to stress.

This interesting finding leads to the question of whether the buffering of evening cortisol is a sign of protection / advantage or a sign of a worn down HPA regulatory system, or allostatic load (McEwen, 2004). Generally, lower cortisol levels in pregnancy are advantageous for healthy pregnancy outcomes. However, a lack of response to adult stress could also indicate an inadequate response to real, existing stressors. The inflection point at which tolerable levels of childhood adversity become non-advantageous has not been determined. The type of stress that leads to adverse outcomes is referred to as "toxic stress". Not all childhood adversity leads to adverse outcomes, with most children showing resilience towards moderate levels of adversity (Shonkoff & Garner, 2012). It may be possible that a clearly defined inflection point does not exist. In other words, there could be levels of stress that are toxic in some respects, yet at the same time advantageous in other ways. For example, while higher cortisol levels in gestation are associated with earlier timing of birth (a disadvantage), higher cortisol levels also promote organ development, especially lung maturation (an advantage). The sample size in this study was not large enough to determine whether the buffered evening cortisol was associated with differential birth or pregnancy outcomes. This question remains for future empirical study.

We also found overlapping influences on the CAR. Whereas high childhood adversity was associated a CAR that was nearly doubled, depression was associated with an elimination of the CAR. Childhood adversity is a risk factor for adulthood depression, and therefore these two experiences are highly co-occurring. We found that women who experienced neither depression nor childhood adversity had almost identical CAR to women who experienced both childhood adversity and current depression. This suggests that although childhood adversity and depression both dysregulate the CAR, there may be separate epigenetic mechanisms working at the same time to both heighten and dampen the CAR. As a result, abused women who are also depressed appear to have a normal CAR related to the overlapping, yet opposite effects of

depression and childhood adversity on the CAR. The possibility for separate etiologic pathways towards depression has been considered, with evidence from genetic studies showing the depression associated with childhood adversity may have more similarity with neurodevelopmental disorders (Malki et al., 2014).

A somewhat related finding is the interaction between adult stress and depression. Women who were not depressed did not show stress-related elevations in cortisol; however depressed women did show elevated cortisol, above and beyond that of depression alone. This could mean that there is an interaction in which cortisol response to stress on a physiologic level is different between depressed and non-depressed individuals. Or this finding could simply be due to depressed individuals experiencing more severe stressors (or at least perceived to be more severe).

We also found that coping interacted with stress on cortisol, such that higher coping was associated with an attenuation of the dysregulating aspects of HPA function noted above. Higher reported use of coping, regardless of the specific strategy, was associated with attenuated cortisol, but only in women who experienced either childhood adversity, high adult stress or depression. In the case of childhood adversity, coping attenuated AUCg in women with high childhood adversity, whereas it did not attenuate cortisol in women without childhood adversity. As noted, childhood adversity was also highly associated with cortisol and the 30 minutes post-awakening time point, which was also attenuated by higher reported use of coping.

In contrast, depressed women who reported more use of coping had higher levels of cortisol in the afternoon. Higher cortisol in women who use more coping could represent women on the lower end of depressive symptoms who have more mental and physical energy to attempt

coping with life demands, whereas women with more severe depressive symptoms may not be able to even mount enough of a cortisol response to respond to stressors. Cortisol is involved in energy mobilization, so it is possible very depressed women do not the physiologic pre-requisites for mobilizing an appropriate coping response to stressors.

Support seeking was a coping strategy that demonstrated the most robust interaction with stress on cortisol, so this strategy was examined further as a sub-category of coping. Women's willingness to seek support buffered high morning cortisol associated with childhood adversity and high evening cortisol associated with adult stress and depression. Willingness to seek support was also linked with a re-setting of a dysregulated CAR associated with depression. Women who were either highly stressed or depressed had attenuated bedtime cortisol levels when they reported more use of support seeking. More use of support seeking was also associated with a normalization of the CAR in depression women. These effects were either not present, or not significant in women without high adult stress or depression. However, this does not mean that coping strategies are not helpful for non-depressed or non-stressed women in other ways. This finding suggests only that coping is not associated with an attenuated HPA response in healthy women. These findings complement other studies examining the moderation effects of environmental factors. Bublitz et al. (2014) found in a longitudinal study over the course of pregnancy that more severe childhood sexual abuse, in conjunction with poor family functioning, was associated with a lack of attenuation of CAR as pregnancy progressed. Better family functioning was associated with a more typical attenuation of CAR as pregnancy progressed.

Seeking support also showed a pattern towards increased length of gestation, possibly by means of its buffering effects on dysregulated cortisol. However, the sample size was not large

enough to detect these effects as significant in a linear regression. Future study of these associations is warranted.

These findings related to the health promoting effects of women's support seeking during pregnancy contributes to the work of nurse researchers who have studied social support as a central concept in nursing for many decades (Norbeck & Tilden, 1983; Tilden, 1983, 1985). These early studies demonstrated that social support for women may not always be uniformly positive, and women may find themselves paying a very high price for comparatively less social support in return (Beeber & Canuso, 2005; Tilden, 1983). Therefore, attention to reciprocity is a key factor in social support warrants further attention in research and clinical practice. Beeber and Canuso (2005) have written about five critical questions to ask women when assessing the strength of women's social support in interventions. These include asking questions addressing instrumental support such as "Who helps you get the day-to-day things you need in your life?", as well as emotional support, such as "Who understands your private worries and feelings?". In the context of an intervention, nurses can play a role in providing both types of social support, while at the same time helping women to map out and expand their social support networks so that the type of support they need is ready and available when they need it.

More recently nurse researchers have integrated principles of social support and interpersonal therapy into nursing interventions with depressed low income mothers (Beeber et al., 2013). For women living in poverty, home visiting is a cost-effective way to engage mothers who otherwise would not engage in mental health interventions (Beil, Beeber, Schwartz, & Lewis, 2013). Beeber has done much work on engaging depressed and impoverished mothers in interventions (Beeber et al., 2007; Beeber, Perreira, & Schwartz, 2008; Beeber & Canuso, 2005). Strategies include focusing on meeting the mother's immediate needs first (e.g. housing, food, health care), assessing readiness for personal change (i.e. not pushing them into interventions

they are not ready for), and providing services in a confidential and non-stigmatizing manner (e.g. based out of Early Head Start programs or home visiting, rather than a psychiatry office) (Beeber et al., 2008).

Our data also suggest that ELA plays an important role in women's responses to stress in pregnancy. Trauma can have long-lasting effects across nearly all aspects of functioning. There have also been interventions developed by nurses to address trauma in holistic ways, including the BE SMART trauma-reframing program (Moller & Rice, 2006). Principles from this program could be used in groups or home visiting interventions with pregnant women with a history of significant trauma or abuse. Pregnancy, especially first-time pregnancy, is a prime time to address depression and the long-term effects of trauma in women. The timing of such interventions could have a significant preventative effect on later maternal-child outcomes and reduce costs associated with these adverse outcomes (e.g. substance abuse, foster care placements, chronic conditions, developmental delay, neurodevelopmental disorders, child delinquency, etc.).

Limitations

The major limitation to this dissertation study was the cross-sectional observational design. This limited our ability to detect differences in cortisol across the length of gestation or associate any of the maternal measures with child outcomes beyond birth. The design did not include an intervention or any alteration of environmental factors based on randomization, which makes it impossible to say whether the associations are causal or otherwise confounded by other unknown factors.

Another limitation was that the sample size was small, and limited the ability to detect some significant differences, such as length of gestation and biophysical measurements of the

newborn. These birth outcomes typically have limited variability (i.e. most newborns are relatively healthy), and therefore it would take a much larger sample size to detect effects on outcomes such as prematurity or low birth weight. Also, it is well-known that the HPA system interacts with various genetic and immune pathways, both within the mother and the fetus. This study did not measure any of the variables to determine whether genetic or immune factors moderate the relationships of interest. The study is also limited in its used of self-report measures. Women may have difficulty recalling events that occurred in the distant past or how they responded to them at the time, and may also be biased their recall based on current stress or depressive symptoms. At this time, the STRAIN is one of the most comprehensive measures of lifetime stress. The options for limiting recall bias are limited outside of longitudinal design.

Summary

In summary, stress over the life course is associated with altered HPA regulation in pregnancy, and women's use of support seeking attenuated the alterations in HPA functioning. Helping women to expand their social support networks may be an effective way of repairing, or re-programming the HPA axis towards normative patterns of functioning, which may have beneficial effects on fetal programming as well. More research is needed to determine whether interventions, such as the ones developed by Beeber, would be effective in restoring healthy biobehavioral and psychosocial adaptive responses in pregnancy, as well as promoting long-term maternal-child mental health.

MANUSCRIPT 3

QUALITATIVE CONSTRUCTIONS OF PREGNANCY HEALTH IN THE CONTEXT OF STRESS AND ADVERSITY

Abstract

The purpose of this study was to explore how pregnant women understand and (de)value health in the context of competing goals and life demands. The study seeks to inform strategies for nurse-delivered interventions during pregnancy. Women's views on health and the strategies used to manage competing life demands and goals were examined via semi-structured interviews during the second half of pregnancy. The study used a grounded theory approach for data analysis and theory construction. Twenty participants were recruited from a large academic medical center in the Midwest at routine prenatal care visits in a women's health center. The emergent findings were constructed around the central phenomenon of *negotiating an imagined future self.* This phenomenon is characterized by a process of approximating the present state of *being many at once*, and the imagined future self of *becoming more*. Women used strategies for managing each of these positions in time. *Undermining contradictions* occur when the strategies to manage *being many at once* do not align with the strategies or goals of *becoming more*. The concept of health was understood broadly by women to represent more than just physical health, and reached across multiple life domains, including financial, relational, social, and emotional health.

Introduction

Pregnancy is a period of enhanced vulnerability for women, especially those who are already in disadvantaged situations. Pregnancy has long been the target of social policy and clinical intervention to improve life course trajectories for both women and children. One of the most promising programs supported by empirical research is the use of nurse home visiting programs during pregnancy (Olds, 2006). The goal of these programs has been to improve maternal-child outcomes in several areas, including prenatal health, pregnancy outcomes, maternal-child interactions, parenting competency, child health and development and maternal life course success (i.e. education, employment, family planning). While these studies have demonstrated quantitative indices of success, SmithBattle (2009) has noted that fewer studies have examined *why* these nurse-delivered interventions have been so successful. She suggests that the success is rooted in the nurse-client interaction that "allows clients to be seen and heard so that their concerns and struggles are mutually discovered and addressed collaboratively" (SmithBattle, 2009, p. 192).

Nurse home visiting interventions have largely relied on social ecological theory (Bronfenbrenner, 1986; Kearney, York, & Deatrick, 2000) . Although this theory has been useful in understanding the ways in which a child's environment at multiple levels affects development, it does not address mothers' agency in shaping an environment for their children, or whether (and to what extant) women are interested in shaping their child's environment.

During pregnancy, the environment of the child is entirely determined by the mother. In no other situation do the lives of two individuals so intimately and closely intertwine than in pregnancy. Factors such as stress and adversity prior to (Guardino et al., 2016) and during pregnancy (Monk et al., 2016) affect the functioning of physiologic mechanisms within the

placenta that influence fetal development. Therefore, on a direct physiologic level, the woman is the child's environment—the way she cares for herself and maintains her own health, therefore is the de facto environment of the child in the first phase of life. Women's health behaviors during pregnancy are therefore a relevant focus for interventions to promote child development *and* maternal health.

Statement of the Problem

Empirical evidence exists defining the predictors, mechanisms and short and long-term outcomes associated with maternal health during pregnancy. However, few studies have examined the topic of health from the perspective of pregnant women. The mother is ultimately the conduit through which any change in this process can take place. She is the one who determines the priorities for her health in pregnancy. Without accounting for how women understand and prioritize health in the context of often complicated and chaotic lives, health promotion interventions risk ineffectiveness. The goal of this research is to develop a theoretical understanding of women's priorities and strategies for managing health in pregnancy. Over the long-term this knowledge can be used to further develop the content and training of nurse-delivered intervention during pregnancy, such as nurse home-visiting programs for vulnerable women.

This paper will describe the findings of the qualitative arm of a mixed methods study looking at the relationship between lifetime stress and health behaviors during pregnancy. The qualitative arm of the study (n = 20) uses a constructivist grounded theory approach (Charmaz, 2014) to examine the meanings of health from the perspective of pregnant women, and to explain how women prioritize health in the context of competing life demands. The quantitative arm of the study examined the relationships between the constructs of lifetime stress,

physiologic cortisol regulation, coping, health behaviors and birth outcomes, but this arm of the study is not described in detail here. The two arms of the study will be analyzed separately, and this paper is a report of the findings from the qualitative arm.

Purpose

The purpose of this qualitative study is to discover how health is understood and (de)valued among competing life priorities by women during pregnancy. The study will explore these meanings in consideration of the assumption that women manage multiple competing life demands during pregnancy. The study will examine how women cope with or integrate these experiences and meanings into their lives. Women's goals and motivations for the future and how they plan to meet those goals are explored. This allowed women to share the ways in which they anticipate coping to prevent or limit the adverse effects of future demands, while accumulating resources allowing them to move positively towards goals and increase personal growth. The findings of this study will be used to inform ways in which nurses could adapt or tailor programs to align better with women's broader life priorities during pregnancy.

Research Question

The central research questions for this study is: How do women understand and (de)value health in the context of competing life priorities during pregnancy?

The sub-questions for the study were:

1. How do women define/understand health and do these ideas about health change in the context of pregnancy?
2. What are women's life priorities during pregnancy and how do they structure these priorities?
3. What strategies do women use to manage the competing life priorities and demands?

Researcher Positioning

Use of a constructivist approach acknowledges that the researcher plays a large role in constructing knowledge about the participants, as much as or more than the participants themselves. Therefore, it is important for researchers to be clear about their positioning and invested interests as they relate to the research being done. My positioning at the time of this writing is as a doctoral student in nursing and a psychiatric-mental health nurse practitioner. I have clinical and research interests in the specialty of perinatal mental health. The study was designed in response to research priorities of the National Institute of Nursing Research (NINR). The NINR Strategic Plan is focused broadly on the "science of health," as opposed to disease. One specific area within this goal is *health promotion and disease prevention*. In the past, nursing interventions targeted health promotion primarily through patient education. However, funding agencies such as NINR now recognize:

> *…successful strategies for health promotion involve more than just educating individuals on healthy living habits. Rather, [nurse] scientists are challenged to determine the collective social and physical behaviors that lead to making healthy lifestyle choices. Health promotion and disease prevention require a thorough exploration of behavior at multiple levels of society, including that of individuals, families, clinicians, health care organizations, communities, and populations" (National Institute of Nursing Research, March 28, 2013).*

Therefore, this research seeks to identify factors that influence health behaviors beyond providing information, and instead consider health behavior within the broader context of women's lives.

As a psychiatric-mental health nurse, I am interested in ways that health institutions and policy can better support women's health and life course trajectory, with an emphasis on

addressing emotional and psychosocial needs. Addressing these issues take both time and resources. Research demonstrating the link between emotional/psychosocial issues and physical health outcomes will further support the value of addressing these issues during pregnancy. Additionally, it is in the interest of health institutions to adopt patient-centered approaches to care. Through these findings, it my hope that consideration of the broader context of women's lives and priorities will enhance emotional and psychosocial health, improve women's satisfaction with pregnancy care, facilitate improved health behaviors, and promote long-term health outcomes and life trajectories for both women and children.

World View

The study is guided by a pragmatist worldview. Creswell (2013) describes pragmatists as doing what works, regardless of the type of method or perspective. Pragmatism is not committed to any one philosophical orientation or method, and often pragmatists will use a mixture of different methods to answer the research question. Pragmatists are realists, believing in a real world outside of the observer, but at the same time recognizing that events occur within different contexts and that subjective meaning matters. In the end, this type of approach is focused on using any methods that will best address the research question. This approach is different from positivist and postpositivist perspectives in that it does not *prioritize* concepts such as reductionism, empiricism, cause and effect orientation, determinism, and use of a priori theories. While a pragmatist might use a postpositivist approach or method, the study would not be limited to these. For the purposes of this research, a pragmatist approach will allow consideration of the research question from multiple angles of inquiry.

The qualitative component of this studied is guided by a social constructivist perspective. This worldview seeks to understand the subjective construction of experience,

complexity and context. The approach is broad and inductive, rather than specific and deductive. Both the research participant and the researcher co-construct knowledge based on prior experience and through the research encounter (Charmaz, 2014). The qualitative arm of the study then will try to make up for what the quantitative part of the study cannot account for—that is the individual, subjective processes, interpretations and meanings of events and circumstances.

Definition of Terms

Health. Within nursing, multiple definitions of health exist. Barrett (Barrett, 2002) reviews these definitions, with one definition being a "cocreated process of *becoming* as experienced and described by the person, family and community" (p. 53). In other words, health is defined by those who experience it. This definition of health is used for the qualitative arm of the study described in this paper by having participants provide their own definition of health. Other definitions include the "physical, psychological, social and spiritual well-being as defined by norms" (p. 53), which is more aligned with the quantitative arm of this study (Chapter 2).

Nursing. The practice of nursing is defined as "the provision of a caring relationship that facilitates health and healing" and attends to the "range of human experiences and responses to health and illness within the physical and social environments" (American Nurses Association, 2010, p. 9).

Nursing Science. Donaldson & Crowley (2002) argue that nursing science is more than a type of nurse-patient interaction, philosophy, theory or methodology. They define nursing science as "the science of personal and familial human health ecology" (p. 61) with a focus on

studying the human response to health or health threats. This definition supports a broader ecological examination of health in pregnancy.

Rationale for Mixed Methods

A mixed methods approach is used in this study in order to draw on the strengths of both quantitative and qualitative research methods. As Creswell (2015) explains, the use of both statistical data (quantitative) and storied data (qualitative) provides a better understanding of the problem than if either method were used alone. The defining features of a mixed methods study include the rigorous use of both quantitative and qualitative methods and the integration of the two types of data using a specific mixed methods design. This study used a convergent mixed methods design. The data was collected concurrently, analyzed separately, and the results will be mixed in the Discussion. While the quantitative arm of the study examines maternal life course adversity from a deductive, stress and coping perspective, the qualitative arm aims for inductive constructions of the meaning and value of health in pregnancy.

Rationale for Constructivist Grounded Theory

Grounded theory (as a more general approach) emphasizes theory construction in an area of knowledge in which little is known. There is little empirical or theoretical literature on the meaning of health among pregnant women or how women's notions of health fit within the broader context of their lives. Although a variety of stakeholders (e.g. health care providers, health organizations) are represented within research and health priorities involving pregnant women, these priorities often overlook the fact that women manage multiple competing life demands during a major life transition. Further, these priorities do not consider that women may define and prioritize health differently than clinicians or health organizations. A grounded

theory approach will facilitate explanation of "varied constructions or competing definitions of the situation" (Charmaz, 2014, p. 322) and generate a substantive theory in this area of inquiry. The inclusion and representation of women's priorities within broader health initiatives may facilitate progress towards improved maternal health during pregnancy.

The specific use of a constructivist approach will be useful because of the emphasis on interpretive meaning that women make of their lives. Rather than discovering the causal processes and consequences that are characteristic of a systematic approach, a constructivist approach will work at uncovering and reconstructing subjective meaning in experience, yet still retain the emphasis on process and action (Charmaz, 2014). The positioning of the researcher within a constructivist worldview is more in line with my own beliefs about knowledge construction, as Charmaz writes "We stand within our research process rather than above, before, or outside it" (p. 321).

Institutional Review Board (IRB) and Ethical Considerations

The study protocol and interview guide were submitted to and approved by the Institutional Review Board. Recruitment began after the IRB approval was received. The researcher collaborated with the clinic staff to identify potential participants. Patients in the clinic were approached by clinic staff, who had ethical access to patients.

The researcher asked all participants permission to audio record the interview. One participant requested that her interview not be recorded. In this case, the researcher took detailed notes, and transcribed the notes immediately after the interview. All other interviews were digitally recorded. Since voice recordings are considered potentially identifiable, these digital voice files were stored on a password-protected, encrypted computer, within a locked

office in the College of Nursing. Hard copy files were stored in a locked file cabinet in the researcher's office. Interview transcripts were de-identified and assigned ID numbers.

Sample Selection

Participants in this study were recruited from a women's health center located within an academic hospital in an urban Midwestern city. The inclusion criteria for this study was based on the criteria for the quantitative study:

Inclusion: a) Single intrauterine pregnancy at least 20 weeks gestation; b) Aged 19 to 45; c) Ability to read and speak English; d) Able to be reached by telephone or text most days of the week.

Exclusion: a) Receiving or referred for care in the high-risk prenatal clinic; b) Have any of the following pregnancy complications or medical issues existing prior to recruitment: cervical or uterine abnormalities, renal, hepatic or cardiac disorders, insulin-dependent diabetes, preeclampsia, regular oral steroid use in the month prior to data collection, congenital fetal abnormalities, active placenta previa, or other disorders/medication use that could affect cortisol levels; c) Regular night-shift work or reversed sleep schedule.

Data collection

Data collection for the qualitative arm of the study consisted of semi-structured interviews. An interview guide (see Appendix E) was developed by the researcher and her advisor. A total of 20 interviews were conducted by the researcher ranging from 18 minutes to 75 minutes, and lasting an average of 45 minutes. One interview was shortened because of the participant's small children being present and in need of her mother's attention. All interviews were conducted face-to-face in a private room either in the women's health clinic or in a research center located in an adjacent building. The researcher took notes during and after the

interviews. Participants received $35 for their time. The quantitative arm of the study consisted of self-report questionnaires, an online structured interview, medical record data and 15 samples of saliva.

Data Analysis

Digital audio recordings were transcribed by a professional transcriptionist. Qualitative data analysis procedures were based on Charmaz's (2014) constructivist grounded theory approach. The researcher began data analysis with open coding using MAXQDA data analysis software and handwritten coding. The researcher read and reread each interview multiple times through. During this process, the researcher elevated several of the initial open codes to categories, and examined the relationships between categories. A central phenomenon emerged, and theory construction was then based around the central phenomenon. A process of constant comparison was used, comparing codes to data, codes to codes, incidents to incidents, codes to categories and categories back to the raw data. Memoing of thoughts occurred throughout the entire research process. An emergent, substantive grounded theory was then reconstructed to describe the process and strategies associated with the central phenomenon. The researcher also kept a methodological journal as part of the memoing process. Journals facilitate the researcher to be reflexive, to write out fleeting thoughts, question assumptions, discover new directions, and to work out dilemmas (Charmaz, 2014).

Findings

A total of 20 women consented to participate in the qualitative arm of the study. Demographic and obstetrical history data are shown in Table 6. These data include age, gestational age, parity, self-identified race, relationship status, education, employment and income. Overall, the sample was varied. Participants ranged in age from 19 to 37 years old, with

a mean age of 26.5 years. Eight participants were nulliparous (had never given birth) while twelve were multiparous (had previously given birth). The sample included ten Caucasian participants and ten African American participants. Most participants were unmarried (70%). Twenty percent were unemployed and seeking work. Household income varied, with 35% of participants reporting a household income of less than $40,00 per year, while 65% were Medicaid insured. Overall, the qualitative sample was from a relatively lower socioeconomic status compared to the sample from the larger quantitative arm of the study. Length of gestation and birth weight were comparable to the full sample, but rates of depression were higher in the qualitative sample (45%) compared to the full sample (30%).

Table 6. Participant characteristics: qualitative study

Participant (N=20) Characteristic	Frequency (%)	Mean ± SD
Maternal Age		26.5 yrs (5.5)
Maternal Race		
White	10 (50%)	
Black or African American	10 (50%)	
Hispanic Ethnicity	0 (0%)	
Completed college (associates or higher)	8 (40%)	
Unemployed, seeking work	4 (20%)	
Married	6 (30%)	
Low Income[1]	7 (35%%)	
Insured by Medicaid	13 (65%)	
Nulliparous	8 (40%)	
History of preterm birth	1 (5%)	
Pre-Pregnancy BMI		26.3 (5.0)
Length of Gestation (days / weeks)		275.6 (11.6) d / 39.4 wks
Birth Weight		3325.8 g (546.6)
Depression[2]	9 (45%)	9 (5.3)

[1] Low Income = Annual household income less than $40,000

[2] Depression was used as a dichotomous variable using a cutoff of 10 or greater on the EPDS

Defining Health

Women in this study were asked about their views on health and how these views might have changed within the context of pregnancy. Many of the women noted the physical aspects of health, such as exercise, diet and avoidance of harmful substances during pregnancy. One woman pregnant with her first child explained that health was more than physical:

> *"Being healthy, I would say not only is a physical thing but being healthy would be a mental and emotional thing. Being happy is being healthy to me. Having support is being healthy and if you want to go physical-wise, exercising and all that, that's health, but if you want to think deeper than physical health, being financially stable is healthy. Being able to provide is healthy. Having support of family is healthy…love is just healthy."*

Because of this participants "deeper" understanding of health, she wanted more from her doctor than just a physical check-up. She explained:

> *I met my doctor one time throughout my whole pregnancy and I'm thinking, okay, I thought I was going to see my doctor every time I came here so we can have that connection because I want this doctor to deliver my baby, so we can have this type of relationship. If they [doctors] could be more… like actually care about how their patients are doing, I feel like they would have…a better outcome. That's why I switched to a [nurse-] midwife."*

Another participant pregnant with her second child described, "I think being healthy is not being stagnant—your mind or your body. And, you know, realizing that what you put in your body is fuel."

Although women were aware of the importance of health, they often did not prioritize it above other life demands, despite recognizing the heightened importance of health in

pregnancy. One participant acknowledged that she doesn't follow her own advice (she works with the mothers of young children). When asked where her health goals fit in with the rest of her life activities, she explained:

> *"My health?...Oh, that's really bottom, which is sad because I know that. I'm logical enough to know—I tell all these parents I work with, 'if you don't take care of yourself, you can't take care of your kids. You can't just keep giving and giving and giving.' My health in general I think I take for granted."*

Negotiating an Imagined Future Self

The central concept *negotiating an imagined future self* (see figure 37) is a process characterized by the movement and development that occurs between a starting point (the present) and an imagined future self. The starting point within this process is *being many at once* and represents the complexity of a present life in which pregnant women fulfill many roles and activities in their present situation. The present is built on foundation of *starting where I came from,* recognizing that women do not start their pregnancy at equal places. Women coming from more disadvantaged background experienced a greater struggle in the present (i.e. homelessness, financial hardships, destructive relationships). The future point is moving and dynamic, and is the imagined mental representation that women have of their lives in the future as mothers and as individuals. This future point is named *becoming more* within the framework, and is composed of women's goals, ideas and motivations for creating a life that they want for themselves and their children. This process of moving forward in time towards imagined goals is not unique to pregnant women. However, pregnancy creates a unique situation characterized by a defined timeline (i.e. 9 months), a new and/or expanding life domain (i.e. new family member), and the accompanying destabilization of the life situation and routine as a result.

Being Many at Once

The category of *being many at once* alludes to the complexity of women's lives, and the many roles and activities that women manage at any one time. These include activities such as supporting a partner, attending to children, helping parents, making money, fulfilling current work responsibilities, parenting younger siblings and managing the expectations of various others. Also existing among these roles and activities is *caring for self*, which is a domain that encompasses physical health and health behaviors. However, because of women's expanded definition of health, this concept is dispersed throughout all domains, including relationships, work, and family. Therefore, "health" is not represented in the model as a singular domain, but spread across all aspects of life. Rather than separate entities, these demands can be overlapping, interacting, contradicting, competing, complementing, or enhancing of one another, as depicted in the following examples.

One participant explained how she works over 50 hours a week in a food service job that doesn't pay as much as she would like, yet she uses her position to access healthy meals that she otherwise might not be able to afford.

> *"[At work] I can make whatever I want, especially because I'm a manager…I can get the best ingredients—I've been really lucky…if I didn't work at a restaurant and I had to buy all my own food—its much harder to eat healthy…I mean, I can eat a $25 salmon with all fresh vegetables for free every day…where somebody else maybe who was pregnant couldn't get a meal like that but once a month, so I'm really grateful for that."*

Another participant has a 9-month-old son and is six months pregnant with her second child. She has made a small business and aspires to become a clothing business owner. She does not have formal childcare for her son, so she must work and care for him at the same time. She

strategically manages her time so that she can also be attentive to her infant son while she works:

> *"I want to make sure I'm spending enough time with him [her son] so usually I'll take him to the park and then put him down for a nap…I'll do all my stuff [work] then, but other times I won't necessarily use the machine. I'll just cut and I'll let him play with the fabrics or something like that so that he's involved, but like, I can still get stuff done."*

Strategies

Women used a variety of strategies to manage the many demands of the present. These strategies included *learning to give up*, *accepting as it is*, *doing what works, and "drawing a line"*. Often these strategies occurred within the context of solving problems within intimate relationships and household responsibilities. One participant, a highly educated woman in her late 30's shared insights about her stubborn tendencies and persistence in keeping relationships that weren't healthy. She explained:

> *"sometimes, I'll stick with it to the death, it seems like, even when it's not the best path…I tried to make it [relationship] work when it was obvious the relationship was not healthy and I was crashing and burning in it…it took him cheating on me in our own apartment and …finding out on my own before I was finally able to be like—"no, this is the end—I have to draw the line somewhere."*

This participant had tried to salvage several bad relationships prior to marrying her husband. With experience and therapy she learned that sometimes its better for relationships to end. So shortly after her first child was born, when her husband wasn't doing his share of the work, she told him "There's the door," drawing on her experience and insight from past relationships "I didn't want it to be like past relationships where I tried to make something work

that wasn't working but I also just didn't have anything left to give, to sacrifice anything else would have been to sacrifice too much of myself for the relationship."

Women in stable, supportive relationships relied on their partners to help manage the demands of life. Another participant, who was in her early 30s, married, and pregnant with her second child, found her husband to be very supportive, especially during times of stress.

> *There's only one day I can think of where I was stressed and then my husband was really supportive, and he was like 'let's get on your running clothes,' I didn't feel like I could fully exert myself running, but, you know, it was helpful that he would go with me and it did help, just getting fresh air and not having to worry about it for a half hour or so.*

However, in some instances, the understanding and support that women needed didn't come naturally to the men in their lives, as a participant described:

> *I think he [her husband] had this delusion that this [pregnancy and parenthood] was just going to be a minor change in our lives and we would just make some minor adjustments and then continue about as business as normal…so it was a really hard shift and it was frustrating for me that he was shifting slower than what I needed him to, as far as picking up the slack on the things that I could just no longer take care of all by myself—I just didn't have enough hours in the day.*

Another participant was in a new relationship when she found out she was pregnant with her second child. She was not confident that the relationship would work out for the long-term, and was hesitant to rely on her partner for helping out:

> *I don't think I would ever actually be able to step down and rely on someone else. I can't do it. I'll take help from [him]…if he wants to pay for something or do this or do that, that's fine, you know? But as far as like my livelihood, putting that*

into somebody else, putting my whole trust into somebody to do that, no way. I have 2 kids, no way…Too much on the line…men are not reliable in my opinion.

Becoming More

The category of *becoming more* represented women's aspirations for the future. Sub-categories included *finding meaning in a career*, *creating and maintaining a mother-child bond*, and *sustaining and supporting a family*. Several of the young mothers had started college, but dropped out for financial reasons. These women were certain of wanting to go back to school to finish their degree. A degree would allow them to attain a career that had personal meaning for them, but would also allow them to financially sustain and support a family, without having to work several jobs at a time.

In order to achieve their goal of *becoming more,* women discussed strategies for rearranging their current life routines and priorities, which often involved going back to school or taking time off work. Women also planned to enlist the help of others, whether it be hired help, or the help of family and friends.

One African American woman in her early 20s pregnant with her first child, had received scholarships to attend a four-year private university, but dropped out after the first year because of family obligations, and also feeling that she did not fit in at the school, being one of only a handful of African-American students. She says of her future career:

I wanted to be a singer and I wanted to be a special education teacher. I wanted to be a therapist, I wanted to be a social worker, I wanted to be an actress, I wanted to be a nurse, I wanted to be an OB/GYN, I wanted to be a lot of stuff…the first thing I ever wanted to do was be a nurse because taking care of people was what I liked to do.

This participant plans to enroll in a community college or an historically black college out of state at some point in the future but does not currently have any specific plans for enrollment. She currently works two low-paying jobs, and says "Just me working two jobs and still feel like I don't have anything...so I'm not having enough to save for myself and for the baby…I wanted to start back in school sometime, I just haven't been able to."

Another participant, a college student who experienced an unstable family life and was placed in foster care as a child also talked about a future career that she would finding meaning in and would allow her to support a family, "I want to go into social work and work with kids. I had a social worker and a therapist as a kid. I could help kids with the same kinds of situations. I know a bit about those kinds of family situations."

Within this category of *becoming more*, women talked about the goals they had for themselves as future mothers (some were already mothers of young children). Overwhelmingly women desired to create stronger connections and provide more support to their own children than they felt was given to them by their own mothers. One participant was raised by a single teenage mother, and understood the challenges her mother endured, though she said "I want to be more" when thinking of herself in relation to her mother. "She [her mother] wasn't' a very emotional person, so I want to kind of be that way [emotional] with my kid…I want to have a bonding relationship… I want to be more involved." Another participant, also born to a teenage mother, and now pregnant with her first child explained:

> *I will always be there for them [her children], which is something I didn't have. I won't give up on them for any reason. I will make sure they always have shelter, food, clothing—no matter what. …everything they need. The basics. And support…if they want to do dancing or sports, even though it will cost, I will figure out how to let them do that.*

Undermining Contradictions

The category of undermining contradictions is both a phenomenon and a process, with the term "undermining" being used as both an adjective and a verb, respectively. As an adjective-phenomenon, it was apparent that some of the strategies that women used to manage the various aspects of the present, worked to undermine future goals for *becoming more*.

One participant illustrated this point in her interview. In addition to undertaking the burden of supporting herself, her two children and providing housing for her partner with her income, she continued to also provide financial support for an abusive ex-boyfriend:

> *I have given him a couple hundred dollars here or there—like for food…I give him money to pay his phone bill. We owe taxes on the [his] house…I'm going to give him $2,500 so we can get that taken care of.*

Although she was adamant that she didn't need a man in her life, she continued to support them financially. Being in her 30s now, she had been in long-term relationships continuously since age 17. The only times she had considered herself alone were when her boyfriends were incarcerated:

> *When the people [boyfriends] I was with were in prison or jail, and I was alone, I was so happy, you know? I was so happy and I did so much in a day. And there was nobody bringing me down, nobody going behind my back—It's just like "I don't ask you for anything. Why do you ask me for like 10 things in a day?"…That's why I think I always accomplished so much when they were out of my hair.*

This participant would like to become a master's prepared social worker. Right now she is nearly finished with her bachelor's degree, but needs to take one last test to finish her credits. She plans to study for the test before she takes it, but cannot do this right now because she

works too many hours at her job. Cutting back on her hours at work, she says, is not an option because she needs the money (much of which is going towards supporting two men who aren't working enough to support themselves). When gently confronted about giving her money away to these men, she said "Well, it's good for me, too, though. If he lost the house, I don't even know where he'd go or what he'd do. It would drive me crazy."

Likewise, another participant did not seek the financial support from the fathers of either of her two young children. At the time of this pregnancy, she was not in a relationship with the father of the baby she was pregnant with. She planned to support the two children on her own, and was not planning to ask for child support. When asked why she did not request child support, she explained:

> *Its not like I don't care, but if you don't want to support your child, I'm not going to make you, you know, because growing up my mom had my dad paying child support and I feel like he didn't really take that out on me–but he was kind of upset. And I just feel like…if you don't want to do it I'm not going to make you do it—I'll be fine.*

Later in the interview, she identified herself as a feminist and spoke about the meaning that this identify has for her.

> *I see a lot of women aren't equal and in a world so consumed with sex when a woman is sexually liberated it's a problem… I feel like feminism today—a lot of people don't understand … it seems like they want women to be how men have been for so long, like, be the top dog, but I really think its just equality. I think equal pay, equal rights… I just feel like a woman should have a right to do what she wants with her body, regardless of what it is honestly…I don't understand the control that men think that they have behind women's bodies is what I am against pretty much.*

Although she believes in the rights of women, it is notable that she does not mention the responsibilities of men. This is not without consequence, as she went on to talk about her aspirations for going back to college. She had recently quit her college program, for which she had received tuition scholarships, because she did not have enough money to buy a computer. She also could not pay for formal childcare arrangements for her children while she studied. Therefore, she is putting her career aspirations on hold for now until she can save enough money to go back to school. Meanwhile, neither father will be giving her any financial support, and she is uncertain whether they will be around at all, "I kinda doubt sometimes that this baby's dad will be there for him, but I'm prepared to deal with it."

As a verb-process, the phrase *undermining contradictions* described the ability for women to hold both the present and future together in their awareness, and pursue strategies that were good both now and in the long-term. This process is a key finding of this analysis, and is a process that nurses working with pregnant women could assess within home visiting programs or other supportive interventions.

Discussion

The findings of this study contribute towards a broader understanding of health in pregnancy by including the perspective of women and how they see health fitting into their lives. Women defined health as being more than their physical selves, and understood that health is more than exercising and eating right. This research supports the idea that personal goals and motivations play a role in shaping health behaviors during pregnancy. The findings support the work of others who note that nurse-patient relationships and interactions with mothers should be more centered on "promoting relationships in which parents expand their awareness of their own and their infant's potential" (Kearney et al., 2000, p. 374) The

theoretical findings of this study could be used to inform the content and approach of nurse-delivered interventions with pregnant women. Nurses could facilitate women clarifying their life priorities and examining whether the strategies that they employ to manage their current situations are in line with reaching longer-term goals.

The conceptions of oneself are important in regulating health behaviors. The notion of a self-concept has been discussed in regard to overall health and nursing research. Self-schemas are the knowledge structures that people construct about themselves, including meaning, motivation, and future goals. They are the "cognitive residual" of the person in interaction with the social environments (Stein, 1995, p. 188). These self-schemas include possible selves, which are linked to current self-schemas. Theories of self-schema parallel our findings here. Women's self-schema's can perhaps be the target of intervention by deconstructing non-useful schemas and constructing new schema's that serve to promote the woman's interests now and in the future (Stein, 1995).

The findings of this study are also in line with the Motivational Theory of Life-Span Development, which emphasizes the adaptive capacity of individuals to optimize self-development during specific life stages in relation to developmentally specific goals (Heckhausen, Wrosch, & Schulz, 2010). Accordingly, pregnancy can be framed in regard to key developmental motivations. One such motivation is that most pregnant women want what is in the best interest of their child. Findings of qualitative studies have suggested that this is a key motivation of many mothers, at least implicitly, regardless of maternal demographics, ability, or illness (Edvardsson et al., 2011), and that it is an innate maternal phenomenon. This motivation is developmentally specific to motherhood and begins during pregnancy with wanting a healthy baby. Within the Motivational Theory of Life-Span Development framework, it is the task of this research to begin to identify the pregnancy-specific processes that facilitate mothers' adaptive

capacity to attain the goal of having a healthy infant via engagement in positive health behaviors, despite stressful or adverse life circumstances. Future clinical interventions can be oriented towards capitalizing on these motivations to engage women in health behavior change.

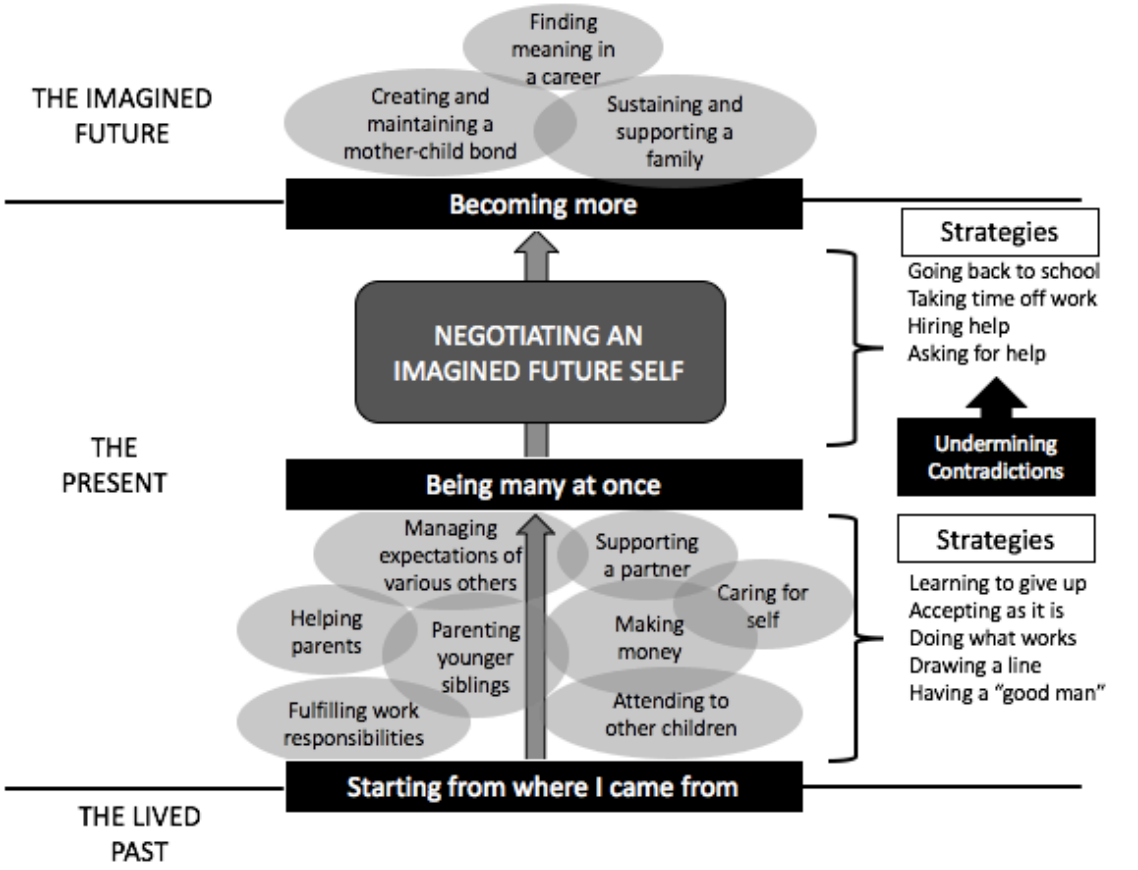

Figure 36. Model of the Process of "Negotiating an Imagined Future Self"

DISCUSSION

The overarching aim of this dissertation study was to explore how maternal adversity over the life course is related to psychosocial and biobehavioral adaptive responses in pregnancy. While many pregnancy studies have focused on current or recent maternal exposure to depression and stressful events in relation to HPA dysfunction (Bussières et al., 2015; Grigoriadis et al., 2013; Palma-Gudiel, Cordova-Palomera, Eixarch, Deuschle, & Fananas, 2015), this study sought to differentiate between more nuanced aspects of adversity over a larger time frame. A measure of stress and adversity over the life course, rather than only recent or current stress was used. This study also included a qualitative research arm in order to examine the situational contexts within which women live, and identify factors that may not have been accounted for in the quantitative instruments.

Early Life Adversity and Prenatal HPA Function

Childhood is a more susceptible period for environmental programming and long term HPA dysregulation. However relatively few studies have examined the association between ELA and physiologic dysregulation of the HPA axis in pregnancy (reviewed in Manuscript 1). Therefore, the purpose of Manuscript 1 was to review the literature on the relationship between maternal ELA and HPA regulation in pregnancy. Nearly all of the 11 studies reviewed found at least one altered aspect of HPA function, although the methods across studies were so diverse that it was difficult to conclude any specific effects, other than that ELA is associated with dysregulated HPA functioning. The reviewed studies demonstrated a heterogeneity of possible effects during pregnancy, including lack of attenuation of CAR and greater increases in CRH towards late gestation.

Lifetime Stress and Prenatal HPA Function

Given the findings of the integrative review, Manuscript 2 examined the association between dimensions of lifetime stress and HPA regulation in pregnancy by accounting separately for childhood adversity, adult stress, and prenatal depression. Although these dimensions of stress are highly inter-correlated, they are separate phenomenon. This analysis found that each of these aspects of maternal adversity and stress have unique association with specific aspects of the diurnal cortisol trajectory over the course of the day. Not only this, but the dimensions of lifetime stress interact to produce different variations of cortisol trajectory. The data suggest that ELA could have a long-term effect on the HPA axis, such that women with ELA do not show a cortisol response to heightened levels of adulthood stress or depression. It is unclear whether this effect is adaptive (i.e. priming for future stress, buffered response) or maladaptive (i.e. inability to mount appropriate response to stress). Although the possibility of mixed adaptive/maladaptive effects is not ruled out.

Coping Attenuates HPA Response in Pregnancy

Aim two of the analysis examined the moderating effect of coping on health behaviors, birth outcomes, and cortisol. After initial analyses, it became clear that childhood adversity was better suited for the role as moderator, rather than coping. Childhood adversity was used as a proxy to represent current altered HPA function, based on the findings of aim one. In women who experienced high childhood adversity, use of more coping was associated with a more normative cortisol trajectory (i.e. lower morning and evening cortisol). The same was true for women who experienced HPA alterations related to depression. More use of coping was associated with a more normative CAR. It is possible that use of more coping has a reparative effect on a dysregulated HPA system.

On the other hand, women who had not experienced high childhood adversity (i.e. no dysregulated HPA function), use of more coping was not associated with cortisol levels. This finding suggests that women's report of more coping is associated with greater normativity of cortisol trajectory, but only in women who had a dysregulated HPA system to begin with. This is not to say that coping is not beneficial in women who did not experience childhood adversity. Rather, these findings only suggest that coping does not alter or shift HPA set-points in healthy women, possibly because their set-points are already at an optimal position. In other words, coping is not going to fix a system that is not broken. This is consistent with another study (Bublitz et al., 2014) in which better family functioning buffered the effects of childhood sexual abuse on cortisol, such that pregnant women with poor current family functioning had increasing CAR over the course of gestation (dysfunctional), whereas women with better current family functioning did not. These findings on coping provide preliminary evidence that HPA dysfunction in pregnant women related to child adversity, stress and depression may be sensitive to re-programming as a result of coping efforts.

Similar findings have been reported in animal studies. Rats that were prenatally stressed responded to an enriched environment with lower glucocorticoids, while for the control rats, the enriched environment did not affect glucocorticoids (Morley-Fletcher et al., 2003). In a similar study, rats who experienced maternal deprivation as infants responded to an enriched environment as adolescents with lower glucocorticoids, but not rats who did not experience maternal deprivation (Francis et al., 2002). These two studies suggest that postnatal enrichment, even into adolescence, is associated with reductions of HPA glucocorticoid reactivity related to early (gestational and early childhood) stress.

In marmosets, higher gestational cortisol exposure in-utero is associated with higher basal cortisol and cortisol reactivity in offspring. As offspring mature in the postnatal environment,

offspring's willingness to initiate play with peers led to decreases in both of those same parameters, basal cortisol and cortisol reactivity. Lowered cortisol occurred across all levels of gestational exposure, but to a greater degree for offspring exposed to higher gestational cortisol. Gestational cortisol prepares the fetus for the external environment, but once there, the offspring is able to continue to adjust and adapt the HPA response in relation to the post-natal environment (Mustoe et al., 2014). The study demonstrated that gestational programming may not be entirely permanent, and in fact is attenuated by increased willingness to initiate and participate in social play.

There is an interesting parallel between the marmoset findings and our findings in pregnant women in that offspring exposed to higher gestational cortisol showed greater reduction in cortisol in response to play. This parallels our findings in pregnant women in that women exposed to higher childhood adversity, stress or depression, experience greater reductions in cortisol associated with coping and support seeking. Together these suggest two important conclusions: 1) Greater basal cortisol and cortisol reactivity (i.e. HPA hyper-reactivity) is susceptible to the reparative effects of positive social interactions and environments, and 2) this is true not only during early childhood years, but during adulthood and pregnancy as well. While these findings imply that reparative effects can occur over the lifespan, there is less known about the extent (i.e. effect size) of these reparative effects at different stages of the human lifespan. Future research might address the following questions: To what extent does early childhood or gestational programming persist into adulthood? Are there periods that are more amenable to attenuation of altered responses? Does the period of attenuation close or expire at some point?

Although our study did not measure HPA reactivity in the newborns or infants, there have been both animal and human studies demonstrating associations between gestational cortisol,

maternal adversity, and offspring HPA reactivity. Abused pregnant women have been shown to have altered cardiac vasovagal responses to challenge (Rice & Records, 2006), and later give birth to newborns who have altered cortisol reactivity to a heel-stick procedure (Rice & Records, 2008).

From an evolutionary perspective, it makes sense that an organism would be able to continuously adapt to the surroundings, and not just predict them in fetal life. The advantage of animal studies is that they can be more highly controlled across all aspects of research, including accuracy in the timing and collection of cortisol samples, and unlimited access to behavior via video recording, neither of which is possible in human studies. Studies in marmosets found that higher gestational cortisol exposure was associated with increased behavioral agitation in offspring at 6 months of age, but disappeared at later stages, perhaps as an adaptation to an environment that is less dangerous than predicted by the mother's high cortisol levels in pregnancy (Mustoe et al., 2014). At the same time, marmosets exposed to higher gestational cortisol engaged in less juvenile play, which acts as a positive social buffer to stress reactivity. Gestational cortisol has both endocrine and behavioral effects on offspring, but both effects are shaped by the postnatal environment, and offspring have the capacity to learn to adjust behavior as appropriate to the environment (Mustoe et al., 2014).

Our data here would suggest that the HPA dysregulation in the form of basal cortisol and cortisol reactivity continues to be malleable into adulthood in women. Although our study was not experimental, it did show association between increased willingness to seek social support and both lower basal cortisol and CAR. This could be used as preliminary data to pursue experimental studies testing the causal effects of interventions targeting improved social networks and help-seeking among women, particularly those with high childhood adversity, high adult stress, or depression.

Differential Susceptibility

Differential susceptibility also plays a role in the extent to which offspring are programed by maternal gestational cortisol exposure such that there are a range of plasticity levels across individuals (Pluess & Belsky, 2010). Certain individuals may be more susceptible to both positive and negative social environments. Bolten (2013) found that gestational cortisol exposure was differentially correlated with infant emotion regulation at 6 months, based on whether infant was high or low reactive to stimulation shortly after birth. This suggests that infants with a more difficult temperament are more susceptible or malleable to change.

Additionally, maternal adversity may program the fetus to have more or less plasticity to the post-natal environment (Pluess & Belsky, 2010). This has led others to argue that maternal adversity prior to or during pregnancy may lead to differential levels of plasticity to the post-natal context, such that women with more stress, adversity, etc., have children who are more susceptible to the effects of postnatal environmental factors such as quality of maternal care and interaction, both positive and negative. Therefore, stratification in future research may be important, as the impact of postnatal interventions may be diluted by sub-groups within the sample who have less potential to benefit from an intervention because of having less plasticity to enriching environmental factors. The same may carry forward into adulthood, and in this case, pregnant mothers.

Stepped-models of care based on levels of risk could be implemented across stratified populations. Grote et al. (2016) found that mothers who were both depressed and had PTSD responded better to an enhanced prenatal depression intervention compared to mothers with only depression. This is in line with our findings that women who have experienced prior trauma during childhood had markedly different HPA axis reactivity than either women with childhood adversity only, or women with depression only. Stratification of interventions could also prove

to be very cost-effective in that more expensive treatments are provided to those who would likely benefit from them the most. In the future, this information could be used to personalize intervention strategies so that a large amount of data (i.e. big data) is not only *predictive* but also *prescriptive*, in terms of what types of treatments should be implemented.

Based on the findings here, the fetal programming hypothesis may be more limited in its scope, and there may be many more ways for the infant, child, and adult brain to be re-programmed (or healed) from early insults or misinformation about the environment during fetal life.

Early Life Adversity and Depression in Pregnancy

Early life adversity and the intergenerational transmission of trauma is one of the main areas of research in the etiology of depressive disorders, along with immune mechanisms and brain processes (e.g. altered neurogenesis, synaptic connections) (reviewed by Menard, 2016). Although not all individuals who experience depression will have experienced significant childhood adversity, ELA is highly prevalent among depressed individuals. In our study, women with high childhood adversity were 5 times more likely to score 10 or greater on the EPDS with 58% of those with ELA scoring at or above this cutoff.

Shalev, Heim and Noll (2016) suggest that the variety of disorders that manifest in relation to a history of childhood maltreatment may be biologically distinct. A variety of pathways towards reduced longevity in these individuals could be related to increased incidence of mental health disorders, poor health behaviors such as smoking and drug use, and the biological embedding of early life adversity (Shalev et al., 2016). Decreased longevity is supported by long-term follow-up studies in women, which have found Increased risk for mortality, that cannot be accounted for by socioeconomic status, personality factors or depression (Chen et al., 2016).

Recent animal studies have addressed the question of the extent of etiologic heterogeneity of depression. Malki et al. (2014) simulated models of endogenous (i.e. non-stress-related) and reactive (i.e. stress-related) models of depression across four different strains of mice. Within the reactively depressed mice, they separately tested early and late life stress. The study found 350 epigenetic changes associated with early life stress and 370 epigenetic changes associated with late life stress. However, there was only an 8.8% overlap between the two stress-related changes associated with early and late life stress. Further, only 30% of this overlap also overlapped with endogenous (non-stress-related) depression. These findings indicate that there may be divergent molecular mechanism underlying the three categories of depression and gene expression for each etiologic category. Furthermore, through the use of gene network analysis, early stress genes were more associated with neurodevelopmental mechanisms, whereas late stress was associated with alterations in cell stress response and signaling. The authors note that it is still possible that there is a final common pathway to depression, regardless of etiology. However, insight into the etiologic molecular and genetic mechanisms might be used in the future to identify the most effective treatments. This is supported by research which found that depression related to more proximal adult stressors is typically more responsive to treatment with pharmacologic therapy (Keers & Uher, 2012).

Furthermore, a meta-analysis of 16 studies found that a history of childhood maltreatment predicted a more unfavorable course of depressive illness, and greater resistance to treatment. Across treatments (therapy, medication or combined treatment), childhood maltreatment predicted decreased response and remission to depression treatment. The authors advocate for screening of childhood maltreatment which could help identify individuals at risk for persistent, chronic, or non-responsive depression and justify more intensive or alternative treatments (Nanni et al., 2012).

In studies of only women (Brown et al., 2007), the most severe levels of childhood maltreatment predicted up to 12 times greater chance of chronic recurrent depression, with greater than a 70% chance of chronic adult depression. Women's experience of maternal lack of affection and rejection had higher odds ratio for depression outcome than physical abuse from the mother or father. This implies that emotional abuse and neglect may have more impact than other types of abuse that typically receive more attention (i.e. physical and sexual abuse). The authors note that sexual abuse rarely occurs without the other types of abuse, and if not controlled for, would more likely be considered a proxy for a larger experience of dysfunction (Brown et al., 2007).

Additionally, adult attachment styles mediate relationship between childhood abuse and neglect and mental health outcomes. Childhood neglect is associated with higher levels of avoidant and anxious attachment in adulthood, which remains relatively stable as a pattern of interpersonal relationships later in life (Widom, Czaja, Kozakowski, & Chauhan, 2017).

On a related note, childhood maltreatment is associated with a 4-fold increased risk for personality disorders, particularly cluster B disorders, with neglect being associated with the widest range of personality disorders (Battle et al., 2004; Johnson, Cohen, Brown, Smailes, & Bernstein, 1999). Gilbert & Widom (2009) argue that neglect is as harmful as physical and sexual abuse, but has received less attention. Aspects of childhood maltreatment that are particularly harmful include low parental affection and nurturing and harsh punishment. The relationship between problematic parental behaviors and risk for personality disorders is graded, such that worse parenting leads to increasingly higher risk for personality disorders (Johnson et al., 1999).

Stressful life events and PTSD also mediate relationship between child adversity and substance abuse in adulthood. Therefore, a triad of depression, personality disorder, and

substance abuse are associated with childhood maltreatment. Poverty also often underlies these problems. Future interventions with women who have experienced clinically significant levels of childhood adversity would need to properly address all of these factors with careful targeting of the intervention (Beeber et al., 2008).

Stress and adverse environmental factors also interact with genetic factors. Polymorphisms in 5-HTTLPR increases susceptibility to stress towards depression. The *S* allele is associated with a stronger susceptibility towards depression in the context of child maltreatment compared to stressful life events later in life (Karg et al., 2011). Response to treatment is also associated with genotype. Morgan et al. (2017) found that the serotonin transporter gene moderated the response to home visiting intervention targeting maternal-infant attachment. The effect size of the intervention for women with SS allele had 2-fold greater increase than controls, while LL carriers had 10-fold decrease in effect size compared to controls. Furthermore, Houtepen et al. (2016) found that KITLG methylation mediates the relationship between childhood adversity and cortisol stress reactivity. Roberts et al. (2015) found that response to psychological therapy was associated with reduced methylation of HPA-related genes. Future research could further examine the interaction between the gene X child maltreatment interaction in relation to treatment outcomes (Keers & Uher, 2012).

The evidence of cortisol as a mediator of maternal adversity on child outcomes is not well established as some have argued for a broader investigation of potential physiologic mediating pathways (O'Donnell & Meaney, 2016). O'Donnell and Meaney (2016) propose that the next step in research is to become more specific with predictors and outcomes in research. This includes specifying the particular characteristics of maternal adversity, and the particular outcomes that are associated with them. Making these distinctions may help elucidate biologic mechanisms within specific situations and sub-groups so that interventions and treatments can

be tailored appropriately. In this research, we have distinguished that cortisol response varies across multiple aspects of maternal adversity (child, adult, depression) in different ways and at different times of the day. This supports the idea that there may be distinct biological mechanism underlying each of these types of maternal adversity. The overlapping of each of these types of adversity, which often occurs, makes it difficult to parse out effects associated with each type of adversity and associated outcomes.

This study provides a starting point to begin to examine different sub-groups of women. In future research, it may be useful to include samples of only depressed or maltreated women. Healthy, non-depressed and non-abused women are likely not going to display variability related to depression scores or stressful events that go beyond the threshold of adversity sufficient enough cause HPA dysfunction. Measuring depressive symptoms in women who do not have clinically significant levels of depressive symptoms is like measuring symptoms of diabetes in people who don't have diabetes. Likewise, looking for biologic correlates of depression (i.e. cortisol) in women who don't have clinically significant depressive symptoms or stress is not helpful. Therefore, in future research it may be useful to limit samples of women to populations that are known to have high risk factors (e.g. Medicaid insured women) or women who meet a cut-off or criteria for a specific condition (e.g. depression).

Qualitative Discussion

The qualitative arm explored the contextual factors associated with health and stress in pregnancy and women's experience of childhood adversity and current life stressors. This arm of the study found that women understand their health as being more than physical to include other domains of life such as emotional health and financial stability. Physical health was not simply a lack of knowledge related to healthy lifestyle, but often had more to do with lack of

time, or the interfering demands of life stressors or poverty. Pregnancy was a time during which women experienced an enhanced motivation to improve their life situations, whether it be getting a job, finding more suitable housing, or furthering their education. Sometimes the strategies that women were using to manage the present life demands undermined their future goals for improvement. The findings of this study could be used to inform the content and approach of nurse-delivered interventions with pregnant women. Nurses could facilitate women clarifying their life priorities and examining whether the strategies that they employ to manage their current situations are in line with reaching longer-term goals.

More recent expansions of these traditional qualitative approaches recognize the heterogeneity of situational factors that could affect both the individual and the process. Methods such as situational analysis (Clarke, 2005) use the situation as the unit of analysis, rather than the individual, the process or the phenomenon. Situational analysis emphasizes taking the contextual circumstances into account, and understanding how these circumstances or positions within a context occur along a spectrum. Not only this, but that many spectral landscapes converge upon one another within any given situation, within any given individual. It is these contextual landscapes which have been overlooked in more traditional approaches to qualitative research, and which I hope to highlight in the future qualitative analysis of this data.

Additionally, I think it is important to consider discourse analyses on pregnancy and health. These studies are unfortunately rarely cited within the biomedical or nursing literature. Discourses on pregnancy, fetuses, and prenatal health are important because they shape the unconscious landscape within which ideas are thought, priorities are set, decisions are made, and actions are taken. Discourse and knowledge go hand in hand with power. Those in power are situated to determine what is legitimate knowledge as it relates to the care of pregnant

women. I hope to incorporate these perspectives in to the future analysis and discussion of this qualitative data.

Topics that will be of particular relevance with regard to future qualitative analyses of this dataset include support seeking, social networks, childhood adversity, and poverty. These topics follow along the lines of the quantitative findings, and could further expand understanding of women's motivations and patterns of seeking social support. A true explanatory mixed-methods design could be carried out using side-by-side tables and analysis of qualitative codes along with quantitative variables using MAXQDA (qualitative software). Qualitative codes could also be ordered along increasing severity of adversity to determine how women's responses change as adversity and stress increase. Use of mixed methods strategies creates a way to integrate the findings of both quantitative and qualitative data to discover patterns that would not have been possible to uncover using either method alone.

Ethical and Social Implications

The impermanence, or re-programmability in the context of environment is an important point to highlight in light of the ethical and social implications of such claims as fetal programming. Some authors have rightly noted that pregnant women in this era are subjected to unprecedented levels of medical and social surveillance and moral judgment (Carolan, 2008; Hammer & Burton-Jeangros, 2013; Coxon, 2014). Within medicine, women's bodies are seen as a constant "risk" to the fetus, which "requires" continuous monitoring and management, especially during labor. Introducing the claim that pregnant women are responsible for the permanent programming of fetal neurodevelopment is potentially a very damaging and harmful sort of discourse to support or contribute to (Lowe, Lee, Macvarish, 2015).

Care must be taken so that this type of research works to benefit women and children, rather than create a scientific justification to blame women and mothers for hindering neurodevelopmental potential of fetuses and children. There are numerous discursive analyses on the topic of surveillance, risk, responsibility and neurodevelopment in pregnancy (Carolan, 2009; Coxon, 2014; Hallgrimsdottir & Benner, 2014; Hammer & Burton-Jeangros, 2013; Jette & Rail, 2014; Lowe, Lee, & Macvarish, 2015; D. Lupton, 2012; D. A. Lupton, 2011; McDonald, Amir, & Davey, 2011). These enlightening analyses draw attention towards the potential (harmful) consequences of scientific findings, or at the least, the potential for misinterpretation of the findings and implications by lay audiences. These discursive analyses have largely originated within the humanities, and have unfortunately not received much citation or attention from those in the sciences, nursing or medicine within the topic area of pregnancy. These discourse analyses will be an area for future reading and discussion.

Contribution to Nursing Science

This research contributes to nursing science by 1) *building the scientific foundation for clinical nursing practice* with mothers and pregnant women, especially towards developing practices that can engage at-risk pregnant women and provide tailored treatment that accommodates the challenges in providing care to marginalized and traumatized populations; 2) *prevent disease and disability* associated with the intergenerational transmission of maternal ELA, HPA dysfunction in pregnancy, and associated socio-emotional effects such as depression and dysfunctional attachment patterns in mothers; and 3) *manage symptoms* of depression and other trauma-related disorders associated with maternal ELA and stress, and improve maternal self-care and health behaviors (National Institute of Nursing Research, 2013).

Intervention

Based on the study findings, women who have experienced high levels of childhood adversity, high adult stress, or depression are at risk for altered HPA function in pregnancy. These areas should be the target of future psychosocial intervention by nurses. There are several important points from this research that are relevant to nursing intervention for these populations of pregnant women.

Nursing. Nurses may be in the best position to provide case management along with trauma-informed therapy approaches. Marginalized populations tend to fear professions that have a reputation for exercising the power to take children away (i.e. social work) or involuntarily committing individuals to a hospital (i.e. psychiatry and other mental health professionals). Generally, nurses do not have a reputation among marginalized women for exercising either of these actions. Additionally, nurse-delivered interventions have consistently demonstrated effectiveness for low income mothers (Beeber et al., 2014; Eckenrode et al., 2010).

Case management. Interventions for impoverished women need to have proper case management built in to the intervention. Good case management, by itself, may be a highly effective intervention (Kneipp et al., 2011). Our findings show that some women may be unwilling to accept or otherwise unable to access instrumental support (i.e. housing, transportation, insurance). They may also live such chaotic lives that maintaining a regular schedule (including attending appointments) may be difficult at best.

Trauma. Women with a history of trauma need a specialized trauma-informed treatment approaches (Moller & Rice, 2006). The long-term effects associated with early life adversity are problems that ideally would be addressed in prenatal care. This is true especially because early

relationships shape long-term patterns of attachment, both to intimate partners and to children. Early life adversity is also highly associated with depression in pregnancy and postpartum. We suggest it would be worthwhile to distinguish between depression that is related to early childhood adversity (negative relationships, altered self-schemas, unwillingness to seek help form others) and depression that is not associated with childhood adversity. Future research should examine how depression interventions might be differentially effective in these two groups of women.

Moller and Rice (2006) provided a model (Figures 1 and 2) demonstrating how trauma transforms an individual's view of the world that is centered around protecting the self from harm, a "me" perspective that self-perpetuates over time. Alternatively, a "we" perspective is one in which life experiences (stressful or not) serve to broaden an individual's worldview. The "we" perspective fosters wellness, health and supports functioning across a variety of life domains, whereas the "me" view generally does not. Thus, the objective of a trauma reframing intervention would be to help women shift from a "me" view to a "we" view. As Moller and Rice (2006) explain: 'When clients no longer define their present based on past experiences, they are well on their way to self-directed wholeness" (p.23).

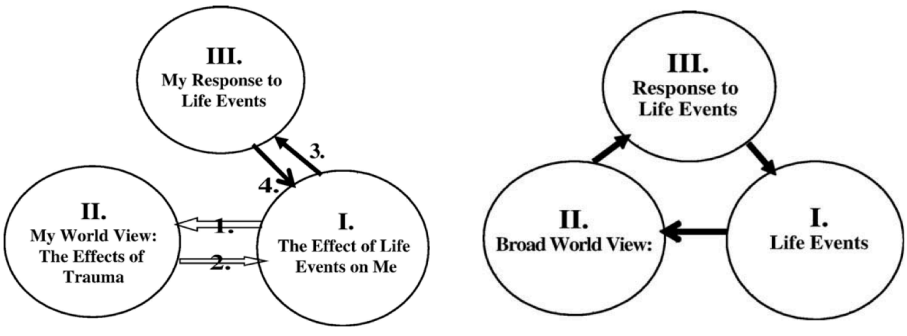

Figure 37. The "me" versus "we" worldviews.
Individuals with a history of trauma tend to take a "me" view, whereas a "we" perspective fosters enhance well-being and health. Shifting from a "me" view to a "we" view is one of the objectives of trauma reframing. (Reprinted with permission).

Substance use. There is a high prevalence of substance abuse among women who have been abused. Residential treatment is extremely difficult to access based on limited availability, especially treatment centers which specialize in and house only women. Even more rare are treatment centers that allow children to stay with their mothers while their mothers receive treatment. Partial substance abuse treatment programs that provide childcare and transportation may be another suitable option. Most mental health intervention research designed for pregnant women or young mothers have left substance abuse issues and treatment completely unaddressed. This cannot be overlooked in future studies.

Depression. Several interventions specific to low-income pregnant women with depression have been developed and tested (Beeber et al., 2014; Grote et al., 2016). As such, there is no need to "re-invent the wheel" with regard to effective depression treatments for low-income pregnant women and mothers. These interventions have used an interpersonal therapy approach, which is in line with our findings that social support is a key target for intervention.

Stepped-Care Models. Future studies could examine how to deliver varying intensities and types of treatments based on the particular symptoms and history that a woman presents with. Also, future interventions might be broadened to include treatment for the triad of depression, substance abuse and personality disorder in women who have experienced significant levels of childhood maltreatment and trauma.

With large samples, algorithms could be developed to determine the most efficient balance between intervention dose, cost and efficacy. Studies with inflexible, standardized designs may not be suitable, considering that nurses in the field are constantly tailoring and adapting their nursing practice towards the needs of the patients. When the population involves low-income women with extremely chaotic and unpredictable lives, it is all the more important that nurses

be allowed flexibility in delivering an intervention. At the same time, it will be important to track, document and study how nursing care is delivered in the context of non-standardized interventions. Future interventions should offer practicing nurses flexibility to make appropriate decisions based on clinical judgment and the needs of the woman.

Support Seeking. Based on our preliminary findings in this study on support seeking, we suggest that this be an area for further research. Women who have experienced early childhood adversity and dysfunctional households may benefit from interventions that include teaching and encouraging women to navigate resources, both formal and informal, in order empower them to advocate for and help themselves. Having a wide base of social support that can be utilized when it is needed is imperative.

Summary

The major finding of this dissertation study is that stress and adversity over the life course are associated with psychosocial and biobehavioral adaptive responses in pregnancy. From a psychosocial perspective, ELA is associated with depression and adult stress. From a behavioral perspective, stress and depression are associated with poor health behaviors (i.e. smoking). From a biologic perspective, ELA, stress and depression are all associated with altered HPA function.

First, we reviewed the literature on HPA dysfunction in pregnancy associated with ELA. A variety of alterations in the HPA diurnal rhythm were noted, as well as changes in response to naturally occurring stressors. Our study findings were consistent with the findings in the review in that we found ELA to be associated with higher cortisol at 30 minutes post-awakening. Adult stress and depression were both associated with higher evening cortisol, and depression was associated with a small or non-existent CAR. The analysis of each of these variables separately

allowed for the identification of unique HPA alterations associated with each type of adversity, which suggests that there may be three differing biological pathways occurring.

Our study builds on previous studies in that we also examined whether coping moderated the relationship between life course stress and cortisol. We found that coping (overall) was associated with a reduction in cortisol levels at the same times of day that were previously found to be elevated in relation to childhood adversity, depression and adult stress, respectively. The coping strategy of support seeking by pregnant women was found to have the strongest interaction effect on the relationship between cortisol and life time stress.

Nursing interventions targeting the enhancement and appropriate use of support seeking is promising area for future research. Give the significant findings in regard to ELA, we believe it is imperative that future research on stress and depression during pregnancy to also take into account women's history of ELA. Women with ELA may be a unique sub-population of women requiring more intensive and assertive treatment. The integration of psychiatric mental health nurses into obstetric care settings could be a novel way to not only improve the value and outcome of care for women, mothers and children, and may also reduce various costs over the long-term associated with preventable outcomes, such as pregnancy interventions (i.e. Cesarean sections), birth outcomes (i.e. neonatal intensive care unit admissions and stays), substance abuse, and inadequate parenting (i.e. foster care placements).

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APPENDICES

Appendix A IRB Approval Letter

University of Nebraska Medical Center

NEBRASKA'S HEALTH SCIENCE CENTER

Office of Regulatory Affairs (ORA)
Institutional Review Board (IRB)

October 26, 2016

Crystal Epstein, MSN
MMI Psychology
UNMC - 5450

IRB # 718-15-EP

TITLE OF PROPOSAL: Stress, Coping and Health Behaviors during Pregnancy

DATE OF EXPEDITED REVIEW: 10/13/2016

VALID UNTIL: 10/13/2017

EXPEDITED CATEGORY OF REVIEW: 45 CFR 46.110; 21 CFR 56.110, Category 3, 7

The UNMC IRB has completed its review of the Application for Continuing Review for the above titled research project including the complete protocol file and has expressed it as their opinion that you have provided adequate safeguards for the rights and welfare of the subjects involved in this study and are in compliance with HHS regulations (45 CFR 46) and FDA regulations (21 CFR 50.56) as applicable.

This letter constitutes official notification of the re-approval of your research project by the IRB for the IRB approval period indicated above. You are therefore authorized to continue this study.

We wish to remind you that, under the provisions of the Federal Wide Assurance (FWA 00002939) from the Institution to HHS, the Principal Investigator is directly responsible for keeping the IRB informed of any proposed changes involved in the procedures or methodology in the protocol and for promptly reporting to the Board any unanticipated problems involving risks to the subjects or others.

In accordance with HRPP policies, this project is subject to periodic review and monitoring by the IRB and, as part of their monitoring, the IRB may request periodic reports of progress and results. For projects which continue, it is also the responsibility of the Principal Investigator to initiate a request to the IRB for Continuing Review of the research project in consideration of the IRB approval period.

On Behalf of the IRB,

Signed on: 2016-10-26 16:57:00.000

Jenny Kucera, MS, CIP
IRB Administrator
Office of Regulatory Affairs

Academic and Research Services Building 3000 / 987830 Nebraska Medical Center / Omaha, NE 68198-7830
402-559-6463 / FAX: 402-559-3300 / Email: irbora@unmc.edu / http://www.unmc.edu/irb

Appendix B Study Recruitment Flyer

University of Nebraska Medical Center

Pregnancy Research Study

This research will survey women's experiences of pregnancy and life stress. Your participation may help future pregnant women like you. You may be eligible to participate if you are…

- Pregnant
- Less than 28 weeks
- Between 19 and 45 years old

This study is observational and will not require you to take medications or change your prenatal care.

You will be compensated for your time.

For more information, please call 402.559.2268 or email crystal.epstein@unmc.edu

IRB# 718-15-EP

Appendix C Table of Quantitative Measures

Construct	Instrument	Description of Measure
Stress	Stress and Adversity Inventory (STRAIN) (25-35 min)	The STRAIN is an online stress assessment administered as a structured interview using computerized intelligent logic to assess 96 different stressors (66 acute life events and 30 chronic difficulties) occurring over an individual's lifetime. There are 220 potential items; irrelevant items are automatically omitted. The STRAIN assesses each stressor's severity, frequency, timing (childhood vs. adulthood), and duration (acute vs. chronic), covering 14 major life domains (housing, education, work, etc.) and 5 social-psychological characteristics (interpersonal loss, physical danger, humiliation, entrapment, role change). Summed scoring for stress exposure (0 to 96) and severity (0 to 480), with higher scores representing higher stressor count and severity, respectively. The validity of this question set has been examined in over 10,000 participants from 32 studies spanning several populations and all age groups. There is predictive validity for physical and mental health symptoms.
	Prenatal Distress Questionnaire (5 min)	The PDQ is a 12-item self-report assessment of pregnancy-specific worries and concerns (e.g., medical complications, physical changes, birth, and health of the baby). Items are rated on a five-point scale (0-4) ranging from "not at all" to "extremely"; summed scores range from 0 to 48, higher scores represent higher pregnancy distress; $\alpha = 0.81$; convergent (STAI Anxiety Scale, Life Event Stress and Perceived Stress) and predictive validity (adverse pregnancy outcomes).
	Salivary Cortisol	Sampling five times daily over three days: awakening, 30 minutes after awakening, 11:00 am, 5:00 pm and 9:00 pm (total 15 samples). Participants document collection of each sample and provide momentary stress ratings in a written log.
Coping	Brief COPE (10 min)	The Brief COPE is a 28-item scale evaluating how frequently a person uses a certain way of coping on a 4-point scale ranging from "I haven't been doing this at all" to "I've been doing this a lot." Summed scores for 14 subscales (active, planning, reframing, accepting, humor, religion/spiritual, seeking emotional support, seeking tangible support, distraction, denial, venting, substance use, disengagement, and self-blame). Two factors identified in pregnant women: active ($\alpha = 0.86$) and disengaged ($\alpha = 0.78$). Convergent and discriminant validity.
Health Behaviors	Health Practices in Pregnancy Questionnaire-II	The HPQ-II is a 34-item self-report questionnaire addressing health practices known to affect pregnancy outcomes in six areas (balance of rest and exercise, safety measures, nutrition, avoiding use of harmful substances, obtaining health care, and obtaining information). Responses range from 1 (never) to 5 (always

Construct	Instrument	Description of Measure
	(HPQ-II) (10 min)	or daily), summed scores range from 34-170; higher scores indicate better health practices. α = 0.81; content and construct validity.
	Prenatal Weight Gain	Weight gain (considered a proxy for healthy diet and exercise) will be evaluated based on the IOM's pregnancy weight gain recommendations (Appendix A8), and will be determined by adjusting for weeks of gestation at the time of weighing.
	Adequacy of Prenatal Care Utilization (APNCU)	The APNCU is a two-factor index based on time of prenatal care initiation and number of prenatal care visits received based on week of gestation; Prenatal care is evaluated as inadequate, intermediate, adequate and adequate plus.
Birth Outcomes	Length of gestation, birth weight	Birth outcome data will be collected from the electronic medical record and analyzed as continuous variables.
Depressive Symptoms	Edinburgh Postnatal Depression Scale (EPDS) (5 min)	The EPDS is a 10-item self-report scale evaluating depressive symptoms over the last 7 days, rated on a 4-point scale (0-3); summed scores range from 0 to 30, with higher scores indicating greater severity of depressive symptoms. A cutoff score of 10 or greater has shown good sensitivity (70%), specificity (96%) and positive predictive value (39%) in pregnant women during the 2nd trimester for depression; α=0.83, test-retest r = 0.63; concurrent validity (Symptom Checklist 90) and predictive criterion validity (CIDI-depression).

Appendix D Survey Instruments

University of Nebraska Medical Center

Pregnancy Research Study: Questionnaires

INSTRUCTIONS:
Please complete this packet of questionnaires. Read the instructions on each questionnaire, and answer the questions to the best of your ability. All of the information you provide will be kept strictly confidential.

Please return these questionnaires in the postage-paid envelope along with your saliva collection kit.

Thank you!

Research Study Contact:
Crystal Epstein, Primary Investigator
University of Nebraska Medical Center
College of Nursing Science
985330 Nebraska Medical Center
Omaha, NE 68198-5330
Office: 402.559.2268
Email: crystal.epstein@unmc.edu

Appendix D-1 Demographic Information

DEMOGRAPHIC INFORMATION

Please respond to the following questions about yourself.

What is your relationship status? (Select one)

- ○ I am married/remarried
- ○ I have a significant other
- ○ I am divorced/separated
- ○ I am widowed
- ○ I am single and never married

What is the highest level of education that you have completed? (Select one)

- ○ Less than 8th grade
- ○ Completed 8th grade
- ○ Completed some high school
- ○ Graduated from high school
- ○ Completed some college
- ○ Completed associates or bachelor's degree
- ○ Completed some graduate school
- ○ Completed graduate or professional degree

Do you have health insurance? (Select one)

- ○ Yes
- ○ No
- ○ Not Sure

What is your current employment status? (Select one)

- ○ Employed full-time (greater than 20 hrs/wk)
- ○ Employed part-time (less than 20 hrs/wk)
- ○ Unemployed, not seeking work
- ○ Unemployed, seeking work
- ○ Student
- ○ Other_____

What is your yearly household income? (Select one)

- ○ Below $10,000
- ○ $10,000 to $19,999
- ○ $20,000 to $39,999
- ○ $40,000 to $59,999
- ○ $60,000 to $79,000
- ○ $80,000 to $99,999
- ○ $100,000 or more
- ○ Prefer not to answer

Do you feel your income is enough to cover your household and living expenses? (Select one)

- ○ Yes, more than enough
- ○ Yes, just enough
- ○ No, not enough

Appendix D-2 Health History

HEALTH HISTORY

Have you ever been told by a health professional that you have any of the following health issues?

Physical Health	**Yes**	**No**
High Blood Pressure or preeclampsia?	☐	☐
If yes, is it treated with medication?	☐	☐
Diabetes? (If yes, select type below)	☐	☐
Gestational	☐	☐
Type I	☐	☐
Type II	☐	☐
If yes, is it treated with medication?	☐	☐
Asthma?	☐	☐
If yes, is it treated with medication?	☐	☐
Musculoskeletal disease?	☐	☐
Liver disease?	☐	☐
Cardiac disease?	☐	☐
Kidney disease?	☐	☐
Thyroid disease?	☐	☐
Migraine?	☐	☐
Epilepsy?	☐	☐
HIV?	☐	☐
Preterm labor in ***this*** pregnancy?	☐	☐
Preterm labor in a ***prior*** pregnancy?	☐	☐
Preterm birth in a prior pregnancy?	☐	☐
Have you ever lost a pregnancy (i.e. miscarriage or stillbirth)?	☐	☐
Other health problems in a ***prior*** pregnancy?	☐	☐
Please list:		
Other health problems in ***this*** pregnancy?	☐	☐
Please list:		

Mental Health	**Yes**	**No**
Depression?	☐	☐
Anxiety?	☐	☐
Bipolar?	☐	☐
Any other mental health problem(s)?	☐	☐
Are you currently receiving treatment or medication for any of these problems?	☐	☐
Please list:		

Medications

Please list all medications you currently take (including prescribed, over the counter, herbal, or vitamin supplements)?

Appendix D-3 Brief COPE

BRIEF COPE

These items deal with ways you've been coping with the stress in your life since you found out you were pregnant. There are many ways to try to deal with problems. Different people deal with things in different ways. Each item says something about a particular way of coping. Please indicate to what extent you've been doing what the item says, and how much or how frequently. Don't answer on the basis of whether it seems to be working or not—just whether or not you're doing it. Try to rate each item separately in your mind from the others. Make your answers as true FOR YOU as you can.

	Not at all	A little bit	A medium amount	A lot
1. I've been turning to work or other activities to take my mind off things.				
2. I've been concentrating my efforts on doing something about the situation I'm in.				
3. I've been saying to myself "this isn't real."				
4. I've been using alcohol or other drugs to make myself feel better.				
5. I've been getting emotional support from others.				
6. I've been giving up trying to deal with it.				
7. I've been taking action to try to make the situation better.				
8. I've been refusing to believe that it has happened.				
9. I've been saying things to let my unpleasant feelings escape.				
10. I've been getting help and advice from other people.				
11. I've been using alcohol or other drugs to help me get through it.				
12. I've been trying to see it in a different light, to make it seem more positive.				
13. I've been criticizing myself.				
14. I've been trying to come up with a strategy about what to do.				
15. I've been getting comfort and understanding from someone.				
16. I've been giving up the attempt to cope.				
17. I've been looking for something good in what is happening.				

	Not at all	A little bit	A medium amount	A lot
18. I've been making jokes about it.				
19. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.				
20. I've been accepting the reality of the fact that it has happened.				
21. I've been expressing my negative feelings.				
22. I've been trying to find comfort in my religion or spiritual beliefs.				
23. I've been trying to get advice or help from other people about what to do.				
24. I've been learning to live with it.				
25. I've been thinking hard about what steps to take.				
26. I've been blaming myself for things that happened.				
27. I've been praying or meditating.				
28. I've been making fun of the situation.				

Appendix D-4 Health Practices in Pregnancy Questionnaire

HEALTH PRACTICES IN PREGNANCY QUESTIONNAIRE

Respond to the answer that best describes your actions since you found out you were pregnant. I know that sometimes you are prevented from doing things the way you planned because of, for example, illness, nausea or medical history. If these special circumstances apply to you, answer questions by thinking about what you did before the problem occurred that required you to change your actions.

	Never	Rarely	Sometimes	Often	Always
1. Since becoming pregnant, I think I am practicing a healthy lifestyle:					
2. Since becoming pregnant, I have gotten at least 7 to 8 total hours of sleep a night:					
3. Since becoming pregnant, I have exercised regularly (for at least 20 minutes a day, at least 3 times per week):					
4. Since becoming pregnant, I have used seatbelts, when available, when driving in a car, truck or van:					
5. Since becoming pregnant, I drink more than 2 caffeinated beverages (coffee, tea, or soda) in a day:					
6. Since becoming pregnant, I have used marijuana:					
7. Since becoming pregnant, I have used methamphetamine, cocaine, crack cocaine, speed, LSD, heroin, or inhalants:					
8. Since becoming pregnant, my partner and/or I have had sex with other people:					
9. Since becoming pregnant, I take actions that reduce my risk for getting sexually transmitted diseases (for example, I have used condoms or avoided intercourse):					
10. When I have concerns about my health or the health of my baby, I report them to my doctor or midwife:					
11. When I have questions about my pregnancy or there is something I don't understand, I ask my doctor or midwife:					
12. Since becoming pregnant, I have taken herbal remedies other than those recommended to me by my doctor or midwife:					
13. Since becoming pregnant, I have read food labels to be sure I am buying an item that will be good for me and my baby (for example, not too high in salt or fat, avoiding artificial sweeteners, and good sources of vitamins):					
14. Since becoming pregnant, I have douched:					
15. Since becoming pregnant, I have avoided bathing or sitting in water that exceeds 100 degrees F:					

	Never	Rarely	Sometimes	Often	Always
16. Since becoming pregnant, I have limited or avoided exposure to toxic chemicals and other substances (for example, second-hand smoke, pesticides/insecticides, lead drinking in water):					
17. Since becoming pregnant, I talk to my doctor or midwife before taking any medication or supplement:					
	Never	1-2 times a week	3-4 times a week	5-6 times a week	Daily
18. Since becoming pregnant, I have taken my multivitamins or prenatal vitamins (if recommended by your doctor or midwife):					
19. Since becoming pregnant, I take in adequate calcium (1200mg/d), by eating dairy products or other calcium-rich foods, or taking supplements:					
20. Since becoming pregnant, I have eaten 5 servings of fruits and/or vegetables in a day:					
21. Since becoming pregnant, I have eaten enough fiber or roughage in my diet (whole grain breads, high fiber cereals, fruits and vegetables):					

FOR THE FOLLOWING QUESTIONS, SELECT ONE ANSWER THAT BEST APPLIES:

22. Since becoming pregnant, I have smoked cigarettes:
    a. Never smoke
    b. Quit since finding out I was pregnant
    c. Less than 10 cigarettes a day
    d. 11 to 20 cigarettes a day
    e. More than a pack a day

23. Since becoming pregnant, I have had alcoholic beverages (wine, beer, or liquor):
    a. No alcoholic drinks while pregnant
    b. Before knowing I was pregnant
    c. Less than 3 times a month
    d. 1 time a week
    e. More than 1 time a week

24. Since becoming pregnant, at one sitting I usually drink (a drink is equal to a 12 ounce bottle of beer, 4 ounces of wine or a shot of liquor):
    a. No drinks while pregnant
    b. 1 drink
    c. 2 drinks
    d. 3 drinks
    e. More than 3 drinks

25. I began seeing my doctor or midwife for prenatal care:
    a. To plan a pregnancy before conception
    b. In the first 3 months of pregnancy
    c. Before 5 months of pregnancy
    d. Before 7 months of pregnancy
    e. Before 9 months of pregnancy

26. Since becoming pregnant, I have: (Missed appointment means forgot to schedule or didn't show up for an appointment with my doctor or midwife):
    a. Never missed an appointment
    b. Missed 1 appointment
    c. Missed 2 to 3 appointments
    d. Missed 4 to 5 appointments
    e. Missed more than 5 appointments

27. Since becoming pregnant, I have gotten regular dental care (professional cleaning every 6 months or dental work):
    a. I do not get regular dental care
    b. I have not been to the dentist even though I am due for dental care
    c. I do not know if I need dental care at this time
    d. I have visited a dentist and had some care but not everything I need
    e. I have visited a dentist and had all dental care done or I am not due for a visit to a dentist since I became pregnant

28. Since becoming pregnant, I have looked at books, pamphlets, videos, or the Internet to learn more about pregnancy and childbirth:
    a. Never
    b. Less than or one time a month
    c. 2 to 3 times a month
    d. 4 times a month (weekly)
    e. More than 4 times a month

29. Since becoming pregnant, I have talked with friends and family members about pregnancy and childbirth:
    a. Never
    b. Less than one time a week
    c. 1 to 2 times a week
    d. 3 to 5 times a week
    e. More than 5 times a week

30. Since becoming pregnant, I have taken time to do something relaxing for myself:
    a. Never
    b. Less than or one time a month
    c. 2 to 3 times a month
    d. 4 times a month (weekly)
    e. More than 4 times a month

31. Since becoming pregnant, I have gained the amount of weight recommended by my doctor or midwife for this time in pregnancy:
    a. I have lost weight
    b. I have gained too little or too much weight
    c. I have not gained or lost weight
    d. I do not know
    e. I have gained the right amount of weight

32. Since becoming pregnant, I drink water, fruit or vegetable juices or other fluids without caffeine daily:
    a. Less than 3 (8oz.) glasses of fluid a day
    b. 3-4 (8oz.) glasses of fluid a day
    c. 5-6 (8oz.) glasses of fluid a day
    d. 7-8 (8 oz.) glasses of fluid a day
    e. More than 8 (8 oz.) glasses of fluid a day

33. Since becoming pregnant, I have minimized my chances of getting toxoplasmosis by avoiding cat feces and not eating raw or undercooked meat and by using gloves when working in the garden:
    a. Always
    b. 5 days a week
    c. 3 days a week
    d. Sometimes
    e. Never

34. I have attended or plan to attend childbirth classes:
    a. No, I have taken them before
    b. Definitely yes
    c. Not sure
    d. Probably not
    e. Definitely no

35. Have you received a flu vaccine in the last year?
    a. Yes
    b. No

36. To the best of your knowledge, how much did you weigh just prior to becoming pregnant?

    _____lbs

37. How tall are you?

    ____ Ft _____ In

Appendix D-5 Edinburgh Postnatal Depression Scale

Edinburgh Postnatal Depression Scale[1] (EPDS)

Name: _____ Address: _____

Your Date of Birth: _____ _____

Baby's Date of Birth: _____ Phone: _____

As you are pregnant or have recently had a baby, we would like to know how you are feeling. Please check the answer that comes closest to how you have felt **IN THE PAST 7 DAYS**, not just how you feel today.

Here is an example, already completed.

I have felt happy:
- ☐ Yes, all the time
- ☒ Yes, most of the time — This would mean: "I have felt happy most of the time" during the past week.
- ☐ No, not very often — Please complete the other questions in the same way.
- ☐ No, not at all

In the past 7 days:

1. I have been able to laugh and see the funny side of things
   - ☐ As much as I always could
   - ☐ Not quite so much now
   - ☐ Definitely not so much now
   - ☐ Not at all

2. I have looked forward with enjoyment to things
   - ☐ As much as I ever did
   - ☐ Rather less than I used to
   - ☐ Definitely less than I used to
   - ☐ Hardly at all

*3. I have blamed myself unnecessarily when things went wrong
   - ☐ Yes, most of the time
   - ☐ Yes, some of the time
   - ☐ Not very often
   - ☐ No, never

4. I have been anxious or worried for no good reason
   - ☐ No, not at all
   - ☐ Hardly ever
   - ☐ Yes, sometimes
   - ☐ Yes, very often

*5 I have felt scared or panicky for no very good reason
   - ☐ Yes, quite a lot
   - ☐ Yes, sometimes
   - ☐ No, not much
   - ☐ No, not at all

*6. Things have been getting on top of me
   - ☐ Yes, most of the time I haven't been able to cope at all
   - ☐ Yes, sometimes I haven't been coping as well as usual
   - ☐ No, most of the time I have coped quite well
   - ☐ No, I have been coping as well as ever

*7 I have been so unhappy that I have had difficulty sleeping
   - ☐ Yes, most of the time
   - ☐ Yes, sometimes
   - ☐ Not very often
   - ☐ No, not at all

*8 I have felt sad or miserable
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Not very often
   - ☐ No, not at all

*9 I have been so unhappy that I have been crying
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Only occasionally
   - ☐ No, never

*10 The thought of harming myself has occurred to me
   - ☐ Yes, quite often
   - ☐ Sometimes
   - ☐ Hardly ever
   - ☐ Never

Administered/Reviewed by _____ Date _____

[1]Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786 .

[2]Source: K. L. Wisner, B. L. Parry, C. M. Piontek, Postpartum Depression N Engl J Med vol. 347, No 3, July 18, 2002, 194-199

Appendix E List of Study Variables

Demographics
- Age
- Non-white
- Hispanic
- Woman of color
- Married
- Significant other
- Completed college
- Unemployed, seeking work
- Low income (<$40,000 household)
- Medicaid insured
- First pregnancy
- Nulliparous
- Has other children
- History of preterm birth

Mental Health
- Takes psychotropic medications
- Self-report of any mental health diagnosis
- Depression score total (EPDS)
- Depression score total (LnEPDS)
- Major depression (EPDS > 10)
- Prenatal distress (PDQ)

Health Behaviors
- Health practices (HPQ-II)
- Pre-pregnancy BMI
- Pregnancy weight gain
- Appropriate pregnancy weight gain
- Smoked during pregnancy
- Continued smoking during pregnancy
- Drank alcohol
- Total prenatal care visits
- Percent of prenatal care visits recommended
- Adequate prenatal care
- Inadequate prenatal care
- Height (m)

STRAIN
- Lifetime stress count
- Lifetime stress severity
- Childhood stress count
- Childhood stress severity
- Adult stress count
- Adult stress severity
- Lifetime stress count (sqrt)
- Lifetime stress severity (sqrt)
- Childhood stress count (sqrt)
- Childhood stress severity (sqrt)
- Adult stress count (sqrt)
- Adult stress severity (sqrt)

Birth Outcomes
- Length of gestation
- < 37 weeks
- < 39 weeks
- < 38 weeks
- Vaginal birth
- Sex of baby
- Birth weight (g)
- Birth length (cm)
- Head circumference (in)
- APGAR 1 minute
- APGAR 5 minutes

Cortisol
- Gestation age at cortisol sampling
- Average daily awake time

Cortisol: Transformed
- Awake (Ln)
- Awake +30 min (Ln)
- Lunch (~12:30 p.m.) (Ln)
- Dinner (~6:30 p.m.) (Ln)
- Bedtime (~10:30 p.m.) (Ln)
- Cortisol awakening response (Ln)
- Slope awake to bedtime (Ln)
- AUCg (Ln)

Cortisol: Raw
Awake
Awake +30 min
Lunch (~12:30 p.m.)
Dinner (~6:30 p.m.)
Bedtime (~10:30 p.m.)
Cortisol awakening response
Slope: awake to bedtime
AUCg

Coping
Denial
Substance use
Distraction
Venting
Active coping
Emotional support
Instrumental support
Behavioral disengagement
Positive reframing
Planning
Humor
Acceptance
Religion
Self blaming
Active coping scale
Disengaged coping scale
Positive coping scale
Negative coping scale
Support seeking scale

Appendix F Tests of Normality

	Statistic	Sig.	Skew z-score	Kurtosis z-score	Normal Histogram
Age	.95	.01	0.02	-2.15	No
Depression score total (EPDS)	.95	.01	2.39	0.04	No
Depression score total (LnEPDS)	.95	.01	-2.27	0.10	Yes
Prenatal distress (PDQ)	.98	.21	0.90	-0.86	Yes
Health practices (HPQ-II)	.99	.61	-0.82	-0.99	Yes
Pre-pregnancy BMI	.91	.00	3.71	1.57	No
Pregnancy weight gain	.96	.03	2.57	1.80	Yes
Total prenatal care visits	.91	.00	-2.97	0.25	No
Percent of prenatal care visits recommended	.94	.00	0.05	3.90	Yes
Height (m)	.99	.60	-0.32	0.51	Yes
Lifetime stress count	.92	.00	3.52	1.62	No
Lifetime stress severity	.89	.00	4.37	2.75	No
Childhood stress count	.79	.00	6.67	7.51	No
Childhood stress severity	.82	.00	5.14	2.91	No
Adult stress count	.89	.00	4.69	4.38	No
Adult stress severity	.87	.00	5.56	5.73	No
Lifetime stress count (sqrt)	.98	.50	0.79	-0.82	Yes
Lifetime stress severity (sqrt)	.99	.75	0.91	-0.11	Yes
Childhood stress count (sqrt)	.95	.01	1.55	0.01	Yes
Childhood stress severity (sqrt)	.96	.02	1.24	-0.86	Yes
Adult stress count (sqrt)	.99	.70	0.41	0.49	Yes
Adult stress severity (sqrt)	.99	.61	0.84	0.58	Yes
Length of gestation	.88	.00	-5.54	6.92	No
Birth weight (g)	.96	.02	-1.91	2.33	Yes
Birth length (cm)	.94	.00	-1.85	5.15	Yes
Head circumference (in)	.91	.00	-4.06	6.34	Yes
Gestation age at cortisol sampling	.97	.08	1.31	1.75	Yes
Average daily awake time	.95	.01	-1.19	0.78	Yes
Awake (Ln)	.98	.52	0.86	2.10	Yes
Awake +30 min (Ln)	.96	.02	-1.13	4.26	Yes
Lunch (~12:30 p.m.) (Ln)	.99	.72	-0.14	-0.62	Yes
Dinner (~6:30 p.m.) (Ln)	.99	.91	0.52	0.43	Yes
Bedtime (~10:30 p.m.) (Ln)	.98	.49	1.52	0.47	Yes
Cortisol awakening response (Ln)	.95	.01	-2.18	3.36	Yes

	Statistic	Sig.	Skew z-score	Kurtosis z-score	Normal Histogram
Slope awake to bedtime (Ln)	.98	.28	1.53	-0.30	Yes
Slope CAR to bedtime (Ln)	.96	.02	2.39	1.94	Yes
AUCg (Ln)	.98	.56	1.17	0.72	Yes
AUCi from bedtime (Ln)	.98	.30	-0.55	-0.83	Yes
AUCi from low value (Ln)	.99	.87	0.27	-0.12	Yes
Awake	.82	.00	8.16	16.28	No
Awake +30 min	.83	.00	8.24	21.14	No
Lunch (~12:30 p.m.)	.93	.00	2.87	0.21	No
Dinner (~6:30 p.m.)	.87	.00	5.99	8.03	No
Bedtime (~10:30 p.m.)	.85	.00	6.20	7.79	No
Cortisol awakening response	.84	.00	-3.74	15.59	No
Slope awake to bedtime	.88	.00	-6.27	11.31	No
Slope CAR to bedtime	.87	.00	-6.29	15.59	No
AUCg	.88	.00	5.65	7.94	No
AUCi from bedtime	.93	.00	4.14	6.99	No
AUCi from low value	.90	.00	5.34	9.73	No
Active coping scale	.97	.12	-1.26	-0.52	Yes
Disengaged coping scale	.86	.00	3.43	2.32	No
Positive coping scale	.97	.14	-0.91	-1.08	Yes
Negative coping scale	.89	.00	3.96	2.85	No
Support seeking scale	.96	.05	-0.87	-1.34	Yes

Appendix G Supplementary Tables

Table 7. Correlations between cortisol and depression

	Depression
Awake (Ln)	**.28***
Awake +30 min (Ln)	.07
Afternoon (~12:30 p.m.) (Ln)	.11
Evening (~6:30 p.m.) (Ln)	**.27***
Bedtime (~10:30 p.m.) (Ln)	.23
Cortisol awakening response (Ln)	**-.27***
Slope awake to bedtime (Ln)	-.01
AUCg (Ln)	**.27***
AUCi from bedtime (Ln)	-.02

Note. Correlation is significant at the 0.05 level (2-tailed).
Control Variables: Age, Low income (<$40,000 household) & Non-white

Table 8. Correlations between health practices and timing of stress (STRAIN)

Pearson Correlation

	Lifetime		Childhood		Adult	
	Count (sqrt)	Severity (sqrt)	Count (sqrt)	Severity (sqrt)	Count (sqrt)	Severity (sqrt)
Health practices (HPQ-II)	**-.38****	**-.30***	-.23	-.17	**-.38****	**-.33****

Spearman's Rho Correlation

	Lifetime		Childhood		Adult	
	Count	Severity	Count	Severity	Count	Severity
Pre-pregnancy BMI	.16	.14	.19	.18	.15	.10
Pregnancy weight gain	-.12	-.08	-.16	-.11	-.09	-.06
Appropriate pregnancy weight gain	-.02	-.04	.10	.09	-.06	-.08
Smoked during pregnancy	.30*	.28*	.01	-.03	.35**	.36**
Continued smoking during pregnancy	.46**	.41**	.05	.03	.51**	.48**
Drank alcohol	.09	.02	.04	-.04	.10	.06
Total prenatal care visits	-.20	-.18	-.12	-.12	-.19	-.17
Percent of prenatal care visits recommended	.01	.07	.07	.09	-.04	.01
Adequate prenatal care	-.08	.00	-.09	-.06	-.03	.01
Inadequate prenatal care	-.16	-.19	-.09	-.11	-.16	-.16
Height (m)	-.10	-.17	-.15	-.17	-.07	-.11

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table 9 Correlations between health practices (HPQ-II) and birth outcomes
Spearman's Rho Correlation

	Length of gestation	< 37 weeks	< 39 weeks	< 38 weeks	Vaginal birth	Sex of baby	Birth weight (g)	Birth length (cm)	Head circumference (in)	APGAR 1 minute	APGAR 5 minutes
Health practices (HPQ-II)	.16	-.04	.00	.07	.13	-.10	.19	-.03	.18	-.03	.11
Pre-pregnancy BMI	-.10	.21	-.01	.03	-.11	.08	-.06	-.04	.06	-.18	-.25*
Pregnancy weight gain	.13	.09	.10	.12	-.09	.11	.30*	.23	.16	-.04	.08
Appropriate pregnancy weight gain	.05	-.10	-.15	-.05	.22	-.23	-.14	-.05	-.11	.10	-.09
Smoked during pregnancy	-.14	.11	.03	.02	-.21	.11	-.06	-.05	.24	-.04	-.04
Continued smoking during pregnancy	-.09	-.07	-.11	.00	-.18	.24	-.11	-.27*	.10	.06	.03
Drank alcohol	.35**	-.13	-.26*	-.17	-.08	.16	.22	.10	.08	.02	.28*
Total prenatal care visits	.58**	-.39**	-.35**	-.29*	-.03	.04	.38**	.24	.41**	.00	.19
Percent of prenatal care visits recommended	-.05	-.25*	.16	.09	.03	.01	.03	-.20	.14	.09	.22
Adequate prenatal care	-.16	-.13	.23	.19	-.17	.03	.05	-.14	.27*	.12	.13
Inadequate prenatal care	.23	.09	-.22	-.26*	.08	.08	-.01	.18	-.17	-.14	-.15
Height (m)	.15	.01	-.16	.01	.22	.00	.43**	.19	.37**	.15	.14

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table 10 Correlation between stress (STRAIN) and birth outcomes
Spearman's Rho Correlation

	Lifetime		Childhood		Adult	
	Count	Severity	Count	Severity	Count	Severity
Length of gestation	.01	-.05	.07	.03	-.05	-.09
< 37 weeks	-.08	-.11	-.05	-.07	-.07	-.14
< 39 weeks	-.21	-.12	-.19	-.14	-.17	-.06
< 38 weeks	-.02	.03	.01	.06	.00	.03
Vaginal birth	-.35**	-.40**	-.30*	-.34**	-.33**	-.31*
Sex of baby	-.01	.01	.09	.13	.00	.03
Birth weight (g)	-.12	-.09	-.08	-.07	-.13	-.09
Birth length (cm)	-.24	-.27*	-.11	-.15	-.28*	-.28*
Head circumference (in)	-.03	-.05	-.19	-.23	.03	.04
APGAR 1 minute	.12	.11	.01	.03	.16	.11
APGAR 5 minutes	.12	.05	.05	.04	.14	.04

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table 11 Correlations between stress (STRAIN) and cortisol (Parametric)
Pearson Correlation

	Lifetime		Childhood		Adult	
	Count (sqrt)	Severity (sqrt)	Count (sqrt)	Severity (sqrt)	Count (sqrt)	Severity (sqrt)
Gestation age at cortisol sampling	.03	-.04	.00	-.02	.05	-.03
Average daily awake time	.07	.05	-.01	-.05	.13	.12
Awake (Ln)	.16	.11	.20	.12	.13	.10
Awake +30 min (Ln)	**.27***	**.25***	**.38****	**.29***	.17	.17
Afternoon (~12:30 p.m.) (Ln)	.03	-.01	.11	.03	-.02	-.06
Evening (~6:30 p.m.) (Ln)	.25	.20	.15	.09	.19	.16
Bedtime (~10:30 p.m.) (Ln)	**.30***	.22	.11	.05	.28*	.21
Cortisol awakening response (Ln)	.11	.16	.19	.19	.03	.08
Slope awake to bedtime (Ln)	.14	.10	-.08	-.06	.16	.11
Slope CAR to bedtime (Ln)	.07	.00	-.20	-.19	.14	.07
AUCg (Ln)	.24	.18	.20	.10	.20	.15
AUCi from bedtime (Ln)	-.14	-.10	.10	.07	-.19	-.15
AUCi from low value (Ln)	-.17	-.14	.02	.00	-.21	-.17

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table 12 Correlations between stress (STRAIN) and cortisol (nonparametric)
Spearman's Rho Correlation

	Lifetime		Childhood		Adult	
	Count	Severity	Count	Severity	Count	Severity
Gestation age at cortisol sampling	.08	.03	.01	-.02	.09	.04
Average daily awake time	.04	.01	.03	.00	.02	.04
Awake	.05	.00	.16	.08	-.02	-.02
Awake +30 min	.24	.18	**.33****	**.26***	.14	.08
Afternoon (~12:30 p.m.)	.03	-.04	.10	.01	-.05	-.09
Evening (~6:30 p.m.)	.18	.11	.12	.07	.12	.09
Bedtime (~10:30 p.m.)	**.26***	.15	.08	.03	.22	.13
Cortisol awakening response	.05	.07	.12	.12	-.01	-.02
Slope awake to bedtime	.03	.04	-.14	-.08	.08	.04
Slope CAR to bedtime	-.10	-.09	**-.29***	**-.25***	.00	.00
AUCg	.19	.11	.20	.11	.10	.04
AUCi from bedtime	-.06	-.09	.18	.11	-.14	-.13
AUCi from low value	-.04	-.09	.18	.10	-.12	-.15

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table 13 Relationship between cortisol and STRAIN (parametric)

	Pearson Correlation (N = 72)	GA at cortisol sampling	Average awake time	Awake (Ln)	Awake +30 (Ln)	Afternoon (Ln) (~12:30 p.m.)	Evening (Ln) (~6:30 p.m.)	Bedtime (Ln) (~10:30 p.m.)	CAR (Ln)	Slope awake - bedtime (Ln)	Slope CAR - bedtime (Ln)	AUCg (Ln)	AUCi from bedtime (Ln)	AUCi from low value (Ln)	Depression (LnEPDS)	Health practices (HPQ-II)
CORE	Physical Health	-.07	-.02	.14	-.03	-.02	.08	.30*	-.22	.13	.27*	.03	-.40**	-.39**	.52**	-.31*
	Mental Health	-.12	.12	.16	-.02	-.19	.15	.28*	-.24	.13	.28*	.05	-.37**	-.35**	.68**	-.40**
	Total Count of Stressors	.03	.07	.16	.27*	.03	.25	.30*	.11	.14	.07	.24	-.14	-.17	.48**	-.38**
	Total Severity of Stressors	-.04	.05	.11	.25*	-.01	.20	.22	.16	.10	.00	.18	-.10	-.14	.46**	-.30*
	Count of Acute Life Events	.04	.04	.15	.22	.06	.28*	.36**	.06	.19	.15	.26*	-.20	-.22	.45**	-.45**
	Count of Chronic Difficulties	.02	.12	.12	.28*	-.01	.17	.18	.19	.08	-.04	.19	-.05	-.11	.47**	-.22
	Severity of Acute Life Events	-.05	.06	.10	.24	.02	.23	.29*	.15	.17	.07	.22	-.16	-.18	.43**	-.36**
	Severity of Chronic Difficulties	-.02	.05	.12	.25*	-.04	.17	.17	.14	.05	-.04	.14	-.07	-.12	.47**	-.25*
TIME LIMITED	Prenatal - Total Count	.11	-.03	.14	.10	.07	.15	.14	-.07	.00	.04	.11	-.06	-.14	.37**	-.24
	Early Adversity Total Count	.00	-.01	.20	.38**	.11	.15	.11	.19	-.08	-.20	.20	.10	.02	.30*	-.23
	Count of Acute Life Events	-.01	-.08	.29*	.44**	.25*	.27*	.25*	.14	-.05	-.14	.31*	.06	.00	.24	-.21
	Count of Chronic Difficulties	.00	.08	.12	.27*	-.02	.01	.01	.17	-.08	-.18	.09	.08	.00	.34**	-.19
	Adulthood - Total Count	.05	.13	.13	.17	-.02	.19	.28*	.03	.16	.14	.20	-.19	-.21	.49**	-.38**
DOMAIN	Housing															
	Acute Life Events	-.08	.14	.00	.24	.02	.26*	.30*	.29*	.28*	.10	.24	-.15	-.17	.36**	-.42**
	Chronic Difficulties	-.02	.09	.11	.21	-.03	.22	.29*	.11	.17	.10	.21	-.18	-.16	.25*	-.35**
	Total Count	-.08	.12	.03	.23	.01	.28*	.32*	.24	.27*	.12	.24	-.18	-.20	.36**	-.44**

Pearson Correlation (N = 72)	GA at cortisol sampling	Average awake time	Awake (Ln)	Awake +30 (Ln)	Afternoon (Ln) (~12:30 p.m.)	Evening (Ln) (~6:30 p.m.)	Bedtime (Ln) (~10:30 p.m.)	CAR (Ln)	Slope awake - bedtime (Ln)	Slope CAR - bedtime (Ln)	AUCg (Ln)	AUCi from bedtime (Ln)	AUCi from low value (Ln)	Depression (LnEPDS)	Health practices (HPQ-II)
Education															
Acute Life Events	-.02	.08	.09	.13	-.09	.02	.04	.03	-.03	-.05	.03	-.05	-.04	.22	-.41**
Chronic Difficulties	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]
Total Count	-.02	.08	.09	.13	-.09	.02	.04	.03	-.03	-.05	.03	-.05	-.04	.22	-.41**
Work															
Acute Life Events	.15	-.03	-.07	.03	-.20	-.13	.01	.13	.06	-.03	-.12	-.16	-.05	.05	-.17
Chronic Difficulties	-.07	.09	-.05	-.06	-.13	.02	.02	-.01	.09	.09	-.04	-.09	-.07	.20	-.06
Total Count	-.03	.04	-.07	-.03	-.16	-.06	-.01	.06	.08	.03	-.08	-.10	-.04	.15	-.11
Treatment/Health															
Acute Life Events	.12	-.07	.05	.19	.05	.04	.14	.16	.07	-.04	.10	-.05	-.08	.15	-.06
Chronic Difficulties	.07	-.06	.22	.32**	.04	.05	.05	.10	-.16	-.22	.09	.05	.05	.22	.02
Total Count	.12	-.04	.22	.36**	.07	.06	.11	.14	-.11	-.20	.15	.04	.02	.22	-.02
Marital/Partner															
Acute Life Events	.06	.10	.16	.02	.04	.19	.26*	-.19	.11	.23	.17	-.18	-.22	.41**	-.35**
Chronic Difficulties	-.09	.15	.00	.06	-.08	.03	.06	.07	.07	.04	.05	-.09	-.15	.35**	-.16
Total Count	.02	.14	.11	.02	-.02	.11	.18	-.13	.09	.17	.12	-.16	-.20	.43**	-.32**
Reproduction															
Acute Life Events	.07	.22	-.13	-.06	-.37**	-.28*	-.22	.10	-.04	-.10	-.21	.00	.03	.09	-.10
Chronic Difficulties	.13	.07	-.02	.06	.02	-.02	-.04	.10	.00	-.06	.06	.11	.14	.02	.17
Total Count	.13	.24*	-.12	-.01	-.31*	-.25*	-.22	.15	-.04	-.13	-.14	.07	.11	.09	.03
Financial															
Acute Life Events	-.16	.01	.04	.16	-.03	.07	.16	.14	.10	.01	.07	-.13	.05	.08	-.28*
Chronic Difficulties	.04	-.09	.12	.16	.18	.40**	.31*	.03	.14	.12	.27*	-.07	-.16	.41**	-.27*
Total Count	-.04	-.06	.08	.17	.10	.29*	.30*	.10	.17	.11	.21	-.15	-.09	.30*	-.32**
Legal/Crime															

Pearson Correlation (N = 72)	GA at cortisol sampling	Average awake time	Awake (Ln)	Awake +30 (Ln)	Afternoon (Ln) (~12:30 p.m.)	Evening (Ln) (~6:30 p.m.)	Bedtime (Ln) (~10:30 p.m.)	CAR (Ln)	Slope awake - bedtime (Ln)	Slope CAR - bedtime (Ln)	AUCg (Ln)	AUCi from bedtime (Ln)	AUCi from low value (Ln)	Depression (LnEPDS)	Health practices (HPQ-II)
Acute Life Events	.05	.08	.04	.10	.05	.14	.11	.07	.07	.03	.16	.03	-.03	.03	-.33**
Chronic Difficulties	-.09	-.08	-.15	-.12	-.09	-.06	-.11	.05	.03	.00	-.14	.00	.00	.13	-.09
Total Count	-.01	.05	-.03	.03	.02	.11	.06	.08	.08	.04	.10	.03	-.03	.10	-.37**
Other Relationships															
Acute Life Events	.03	.08	.10	.09	.01	.21	.18	-.02	.09	.11	.15	-.08	-.11	.14	-.08
Chronic Difficulties	-.10	.12	.11	.24	.04	.16	.17	.14	.07	-.02	.20	-.02	-.09	.50**	-.23
Total Count	-.06	.13	.09	.22	.02	.20	.20	.15	.11	.02	.21	-.05	-.13	.48**	-.21
Death															
Acute Life Events	.02	-.17	.04	.12	.09	.22	.21	.10	.11	.05	.14	-.08	-.12	.19	-.09
Chronic Difficulties	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]
Total Count	.02	-.17	.04	.12	.09	.22	.21	.10	.11	.05	.14	-.08	-.12	.19	-.09
Life-Threatening Situations															
Acute Life Events	-.10	-.04	.23	.21	.10	.14	.25*	-.06	.02	.05	.18	-.13	-.15	.37**	-.25*
Chronic Difficulties	-.05	-.09	.10	.05	-.04	.09	.20	-.07	.07	.11	.04	-.21	-.23	.26*	-.15
Total Count	-.11	-.08	.20	.18	.08	.14	.25*	-.05	.03	.06	.15	-.15	-.17	.36**	-.27*
Possessions															
Acute Life Events	.14	.06	.06	.14	.00	.19	.21	.09	.13	.07	.15	-.14	-.15	.05	-.01
Chronic Difficulties	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]
Total Count	.14	.06	.06	.14	.00	.19	.21	.09	.13	.07	.15	-.14	-.15	.05	-.01
Interpersonal Loss															
Acute Life Events	-.02	-.03	.09	.07	.02	.21	.22	-.04	.11	.14	.14	-.12	-.15	.36**	-.18
Chronic Difficulties	-.15	.13	.06	.12	-.03	.10	.12	.06	.07	.03	.12	-.07	-.14	.42**	-.28*
Total Count	-.07	.04	.09	.10	-.02	.18	.20	.01	.11	.11	.15	-.12	-.17	.43**	-.22

Pearson Correlation (N = 72)	GA at cortisol sampling	Average awake time	Awake (Ln)	Awake +30 (Ln)	Afternoon (Ln) (~12:30 p.m.)	Evening (Ln) (~6:30 p.m.)	Bedtime (Ln) (~10:30 p.m.)	CAR (Ln)	Slope awake - bedtime (Ln)	Slope CAR - bedtime (Ln)	AUCg (Ln)	AUCi from bedtime (Ln)	AUCi from low value (Ln)	Depression (LnEPDS)	Health practices (HPQ-II)
Physical Danger															
Acute Life Events	-.01	.03	.21	.24	.05	.16	.33**	.00	.10	.10	.23	-.20	-.25*	.44**	-.38**
Chronic Difficulties	.00	.05	.06	.20	-.07	.12	.26*	.16	.18	.08	.14	-.20	-.19	.19	-.26*
Total Count	-.01	.04	.18	.24	.00	.13	.31*	.05	.12	.09	.20	-.21	-.23	.40**	-.37**
Humiliation															
Acute Life Events	.17	.02	.05	.04	-.04	.07	.16	-.01	.10	.10	.05	-.19	-.16	.27*	-.35**
Chronic Difficulties	-.04	.19	-.01	.16	-.02	.13	.21	.21	.22	.10	.18	-.13	-.20	.35**	-.11
Total Count	.05	.16	.04	.14	-.01	.15	.25*	.11	.20	.13	.18	-.18	-.20	.36**	-.32**
Entrapment															
Acute Life Events	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a	.a
Chronic Difficulties	-.04	.06	.18	.21	.05	.21	.14	.02	-.02	-.03	.20	.04	.02	.48**	-.24
Total Count	-.04	.06	.18	.21	.05	.21	.14	.02	-.02	-.03	.20	.04	.02	.48**	-.24
Role Change/Reversal															
Acute Life Events	-.07	.08	.05	.26*	.09	.30*	.33**	.26*	.25*	.09	.28*	-.13	-.13	.32*	-.48**
Chronic Difficulties	.09	-.08	.05	.17	-.08	.01	-.04	.15	-.09	-.18	-.04	.03	.03	.29*	.05
Total Count	.01	.03	.09	.31*	.05	.26*	.21	.24	.11	-.05	.21	-.04	-.04	.38**	-.34**

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

a. Cannot be computed because the STRAIN variable is equal to 0.

Table 14 Cortisol and STRAIN (nonparametric)

	Spearman's Rho Correlation (N = 72)	Gestation age at cortisol sampling	Average awake time	Awake	Awake +30 min	Afternoon (~12:30 p.m.)	Evening (~6:30 p.m.)	Bedtime (~10:30 p.m.)	Cortisol awakening response	Slope awake to bedtime	Slope CAR to bedtime	AUCg	AUCi from bedtime	AUCi from low value	Takes psychotropic medications	Self-report of any MH diagnosis	Depression score total (EPDS)	Depression score total (LnEPDS)	Major depression (EPDS > 10)	Health practices (HPQ-II)
CORE	Physical Health	-.05	-.06	.10	-.07	.00	-.02	.24	-.28*	-.01	.19	-.03	-.32**	-.30*	.05	.24	.57**	.58**	.56**	-.24
	Mental Health	-.10	.10	.14	-.06	-.19	.11	.19	-.24	-.03	.16	-.06	-.32**	-.32**	.18	.41**	.71**	.71**	.63**	-.39**
	Total Count of Stressors	.08	.04	.05	.24	.03	.18	.26*	.05	.03	-.10	.19	-.06	-.04	-.01	.13	.48**	.49**	.45**	-.34**
	Total Severity of Stressors	.03	.01	.00	.18	-.04	.11	.15	.07	.04	-.09	.11	-.09	-.09	.06	.22	.52**	.49**	.48**	-.30*
	Count of Acute Life Events	.08	-.03	.01	.20	.05	.19	.31*	.04	.08	-.05	.19	-.10	-.07	-.08	.10	.42**	.44**	.40**	-.38**
	Count of Chronic Difficulties	.09	.10	.03	.22	-.02	.12	.11	.11	.02	-.14	.15	-.01	-.02	.10	.16	.48**	.49**	.43**	-.23
	Severity of Acute Life Events	.00	.02	.00	.20	-.01	.13	.21	.05	.07	-.08	.15	-.10	-.08	-.03	.18	.46**	.44**	.46**	-.32**
	Severity of Chronic Difficulties	.06	.00	.01	.16	-.03	.11	.10	.07	.00	-.12	.10	-.06	-.07	.14	.24*	.52**	.49**	.45**	-.24*
TIME-LIMITED	Prenatal - Total Count	.06	.00	.10	.14	.04	.14	.12	-.11	-.05	-.05	.13	-.02	-.03	.12	.27*	.32**	.37**	.26*	-.22
	Early Adversity																			
	Total Count	.01	.03	.16	.33**	.10	.12	.08	.12	-.14	-.29*	.20	.18	.18	-.04	.06	.31*	.34**	.32**	-.24*
	Count of Acute Life Events	-.03	-.04	.24	.40**	.27*	.24	.22	.10	-.16	-.33**	.36**	.25*	.29*	-.14	-.01	.25*	.28*	.28*	-.20
	Count of Chronic Difficulties	.03	.09	.11	.26*	-.03	.00	.02	.13	-.10	-.23	.10	.09	.07	.04	.09	.33**	.35**	.29*	-.19
	Adulthood - Total Count	.09	.02	-.02	.14	-.05	.12	.22	-.01	.08	.00	.10	-.14	-.12	.02	.17	.46**	.47**	.41**	-.30*
DOMAIN	*Housing*																			
	Acute Life Events	-.06	.09	-.07	.13	.00	.18	.24	.21	.18	-.03	.14	-.11	-.09	-.11	.15	.39**	.35**	.36**	-.41**
	Chronic Difficulties	-.05	.07	.04	.23	-.02	.17	.27*	.12	.03	-.09	.18	-.05	.00	-.12	-.05	.24*	.27*	.26*	-.33**
	Total Count	-.06	.06	-.07	.14	-.03	.18	.25*	.18	.16	-.02	.13	-.13	-.10	-.13	.11	.37**	.35**	.34**	-.40**
	Education																			
	Acute Life Events	-.01	.06	.06	.08	-.09	.01	.02	.03	-.04	-.03	.02	-.04	-.03	.02	.09	.24	.21	.27*	-.38**
	Chronic Difficulties	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	Total Count	-.01	.06	.06	.08	-.09	.01	.02	.03	-.04	-.03	.02	-.04	-.03	.02	.09	.24	.21	.27*	-.38**
DOMAIN	*Work*																			
	Acute Life Events	.15	-.05	-.08	.06	-.22	-.14	.01	.11	.04	-.08	-.08	-.15	-.12	.01	.13	.14	.11	.21	-.17
	Chronic Difficulties	-.08	.11	-.04	-.11	-.12	-.01	-.02	-.15	.02	.10	-.08	-.12	-.14	.05	.22	.28*	.23	.26*	-.04
	Total Count	-.02	.04	-.07	-.05	-.16	-.09	-.03	-.03	.03	.02	-.09	-.13	-.12	.05	.20	.23	.18	.25*	-.10
	Treatment/Health																			
	Acute Life Events	.15	-.12	-.01	.22	.02	.00	.14	.14	.00	-.17	.11	-.02	-.02	.15	.29*	.20	.17	.18	-.04

Spearman's Rho Correlation (N = 72)	Gestation age at cortisol sampling	Average awake time	Awake	Awake +30 min	Afternoon (~12:30 p.m.)	Evening (~6:30 p.m.)	Bedtime (~10:30 p.m.)	Cortisol awakening response	Slope awake to bedtime	Slope CAR to bedtime	AUCg	AUCi from bedtime	AUCi from low value	Takes psychotropic medications	Self-report of any MH diagnosis	Depression score total (EPDS)	Depression score total (LnEPDS)	Major depression (EPDS > 10)	Health practices (HPQ-II)
Chronic Difficulties	.15	.05	.15	.30*	-.01	.04	-.01	.07	-.15	-.31*	.15	.11	.14	.40**	.22	.23	.23	.28*	.01
Total Count	.20	-.02	.14	.35**	.05	.06	.10	.11	-.14	-.33**	.20	.10	.12	.35**	.28*	.27*	.26*	.29*	.01
Marital/Partner																			
Acute Life Events	.13	.08	.12	.05	-.01	.12	.19	-.26*	-.03	.08	.07	-.13	-.14	.01	.18	.40**	.43**	.44**	-.26*
Chronic Difficulties	-.04	.15	-.04	.06	-.07	.02	.03	-.02	.09	.01	.02	-.10	-.12	-.09	.01	.40**	.36**	.27*	-.11
Total Count	.10	.11	.04	.03	-.07	.03	.11	-.20	.01	.08	.01	-.14	-.16	-.04	.13	.44**	.45**	.40**	-.24
Reproduction																			
Acute Life Events	.12	.21	-.13	-.12	-.38**	-.34**	-.24	.08	.05	.07	-.25*	-.15	-.19	-.02	.07	.09	.08	.04	-.11
Chronic Difficulties	.17	.07	-.03	.05	.03	-.04	-.06	.14	.03	-.04	.04	.03	.06	.04	-.02	.07	.06	.13	.17
Total Count	.21	.23	-.12	-.06	-.30*	-.31*	-.25*	.15	.06	.03	-.18	-.10	-.12	.01	.04	.13	.10	.13	.03
Financial																			
Acute Life Events	-.19	-.02	.01	.11	-.01	.06	.13	.12	-.01	-.08	.08	-.02	.06	-.15	.08	.19	.18	.25*	-.28*
Chronic Difficulties	.03	-.14	.05	.16	.18	.37**	.27*	.06	.03	-.07	.26*	.04	.02	.09	.12	.38**	.41**	.32**	-.26*
Total Count	-.06	-.11	.01	.15	.10	.28*	.27*	.11	.06	-.06	.20	-.02	.02	.01	.11	.33**	.35**	.33**	-.31*
Legal/Crime																			
Acute Life Events	.11	.07	-.12	.11	.02	.10	.08	.17	.17	-.02	.11	.05	.03	-.15	.08	-.01	-.03	.05	-.26*
Chronic Difficulties	-.06	-.10	-.18	-.16	-.12	-.09	-.10	.00	.10	.12	-.18	-.12	-.14	.09	.05	.15	.14	.09	-.08
Total Count	.02	.03	-.19	.01	-.02	.06	.03	.13	.21	.05	.02	-.01	-.03	-.07	.12	.10	.08	.12	-.32**
Other Relationships																			
Acute Life Events	-.01	.03	.09	.17	-.01	.17	.12	-.05	.01	-.09	.14	.00	.03	-.20	.05	.18	.16	.20	-.06
Chronic Difficulties	.04	.11	.07	.20	.03	.14	.14	.15	.00	-.11	.16	.03	.02	.00	.03	.44**	.46**	.38**	-.23
Total Count	.05	.10	.06	.22	.02	.16	.16	.14	.02	-.12	.18	.02	.01	-.04	.04	.44**	.45**	.37**	-.23
Death																			
Acute Life Events	.04	-.18	-.02	.14	.06	.16	.13	.10	.05	-.05	.16	.00	.03	-.08	-.03	.17	.20	.16	-.04
Chronic Difficulties	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
Total Count	.04	-.18	-.02	.14	.06	.16	.13	.10	.05	-.05	.16	.00	.03	-.08	-.03	.17	.20	.16	-.04
Life-Threatening Situations																			
Acute Life Events	-.09	-.04	.13	.12	.11	.07	.19	-.19	-.08	-.03	.12	-.06	-.03	-.12	-.06	.36**	.41**	.38**	-.18
Chronic Difficulties	-.07	-.08	.11	.10	-.05	.08	.16	-.16	-.03	-.02	.09	-.14	-.10	-.21	.05	.23	.28*	.34**	-.13

Spearman's Rho Correlation (N = 72)		Gestation age at cortisol sampling	Average awake time	Awake	Awake +30 min	Afternoon (~12:30 p.m.)	Evening (~6:30 p.m.)	Bedtime (~10:30 p.m.)	Cortisol awakening response	Slope awake to bedtime	Slope CAR to bedtime	AUCg	AUCi from bedtime	AUCi from low value	Takes psychotropic medications	Self-report of any MH diagnosis	Depression score total (EPDS)	Depression score total (LnEPDS)	Major depression (EPDS > 10)	Health practices (HPQ-II)
CHARACTERISTIC	Total Count	-.11	-.08	.10	.10	.08	.07	.18	-.19	-.05	-.01	.09	-.09	-.06	-.15	-.04	.33**	.39**	.38**	-.21
	Possessions																			
	Acute Life Events	.16	.06	.10	.18	.01	.16	.16	.11	.02	-.09	.17	-.06	-.01	.04	-.02	.03	.01	.02	-.02
	Chronic Difficulties	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	Total Count	.16	.06	.10	.18	.01	.16	.16	.11	.02	-.09	.17	-.06	-.01	.04	-.02	.03	.01	.02	-.02
	Interpersonal Loss																			
	Acute Life Events	.03	-.08	.03	.14	-.02	.15	.17	-.03	.03	-.01	.14	-.03	-.01	-.08	.10	.30*	.31*	.28*	-.11
	Chronic Difficulties	-.10	.16	.00	.09	-.02	.08	.11	-.04	.05	-.01	.07	-.07	-.09	-.08	.02	.47**	.44**	.34**	-.25*
	Total Count	.02	-.01	.01	.14	-.03	.16	.19	-.03	.06	-.01	.13	-.06	-.06	-.08	.10	.40**	.41**	.36**	-.16
	Physical Danger																			
	Acute Life Events	.01	.00	.11	.22	.04	.10	.28*	-.06	-.04	-.07	.19	-.10	-.08	-.07	.12	.43**	.46**	.40**	-.32**
	Chronic Difficulties	.02	.04	-.03	.19	-.10	.07	.22	.11	.09	-.08	.11	-.14	-.10	-.16	.01	.14	.19	.18	-.21
	Total Count	.02	.01	.08	.22	.00	.08	.27*	-.03	-.02	-.07	.16	-.11	-.09	-.08	.10	.38**	.42**	.37**	-.31*
	Humiliation																			
	Acute Life Events	.20	.00	-.02	.06	-.05	.05	.12	-.04	.06	.01	.01	-.14	-.14	.02	.11	.29*	.28*	.33**	-.30*
	Chronic Difficulties	.03	.15	-.01	.18	-.05	.10	.18	.15	.11	-.05	.12	-.08	-.08	-.02	.10	.32**	.34**	.35**	-.13
	Total Count	.13	.13	.00	.16	-.02	.14	.22	.06	.09	-.03	.12	-.09	-.08	-.04	.08	.37**	.37**	.39**	-.30*
	Entrapment																			
	Acute Life Events	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
	Chronic Difficulties	.02	.02	.13	.18	.09	.23	.16	.06	-.10	-.13	.22	.07	.06	.11	.09	.49**	.48**	.38**	-.27*
	Total Count	.02	.02	.13	.18	.09	.23	.16	.06	-.10	-.13	.22	.07	.06	.11	.09	.49**	.48**	.38**	-.27*
	Role Change/Reversal																			
	Acute Life Events	-.03	.02	-.06	.18	.09	.24	.27*	.20	.17	-.05	.18	-.06	-.03	-.15	.10	.37**	.34**	.37**	-.43**
	Chronic Difficulties	.11	.02	.01	.17	-.08	-.01	-.11	.05	-.06	-.21	.02	.04	.04	.34**	.23	.37**	.36**	.37**	.01
	Total Count	.02	.02	-.02	.22	.06	.17	.14	.19	.08	-.16	.15	.00	.04	.09	.18	.44**	.41**	.41**	-.32**

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table 15 Relationship between Cortisol and Birth Outcomes

Spearman's Rho Correlation (N = 72)	Length of gestation	< 37 weeks	< 39 weeks	< 38 weeks	Vaginal birth	Female sex of baby	Birth weight (g)	Birth length (cm)	Head Circ. (in)	APGAR 1 minute	APGAR 5 minutes
Gestation age at cortisol sampling	.19	-.19	-.24	-.31*	-.11	-.04	-.20	-.13	.11	-.03	-.11
Average daily awake time	.02	-.13	-.07	-.19	-.01	-.14	.02	.15	.00	-.05	.08
Awake (Ln)	-.05	-.05	.08	.25*	.12	.23	.05	.22	.00	.12	-.05
Awake +30 min (Ln)	.12	-.29*	-.27*	-.04	-.12	.03	.20	.14	.11	.23	.13
Afternoon (~12:30 p.m.) (Ln)	-.05	-.17	.14	.16	.14	.08	-.06	-.08	-.18	.11	.04
Evening (~6:30 p.m.) (Ln)	.07	-.08	-.13	.18	.13	-.02	.03	-.03	-.01	-.08	-.15
Bedtime (~10:30 p.m.) (Ln)	.03	.00	-.11	.03	.17	.05	-.01	.08	.02	-.03	-.03
Cortisol awakening response (Ln)	.10	-.27*	-.36**	-.40**	-.22	**-.30***	.11	-.04	.07	.13	.11
Slope awake to bedtime (Ln)	.12	.01	-.20	-.30*	.00	**-.27***	-.04	.02	.03	-.15	.05
Slope CAR to bedtime (Ln)	-.01	.14	.05	-.07	.21	-.04	-.18	.01	-.09	-.16	-.02
AUCg (Ln)	-.01	-.17	-.10	.05	.07	-.05	-.01	.02	-.07	.14	.08
AUCi from bedtime (Ln)	-.06	-.26*	.05	.03	-.11	-.07	-.01	-.13	-.05	.14	.02
AUCi from low value (Ln)	-.07	-.29*	.05	.00	-.12	-.06	.07	-.06	.02	.19	.08
Awake	-.05	-.05	.08	.25*	.12	.23	.05	.22	.00	.12	-.05
Awake +30 min	.12	-.29*	-.27*	-.04	-.12	.03	.20	.14	.11	.23	.13
Afternoon (~12:30 p.m.)	-.05	-.17	.14	.16	.15	.08	-.06	-.08	-.18	.11	.04

Spearman's Rho Correlation (N = 72)	Length of gestation	< 37 weeks	< 39 weeks	< 38 weeks	Vaginal birth	Female sex of baby	Birth weight (g)	Birth length (cm)	Head Circ. (in)	APGAR 1 minute	APGAR 5 minutes
Evening (~6:30 p.m.)	.07	-.08	-.13	.18	.13	-.02	.03	-.03	-.01	-.08	-.15
Bedtime (~10:30 p.m.)	.03	.00	-.11	.03	.17	.05	-.01	.08	.02	-.03	-.03
Cortisol awakening response	.12	-.26*	-.40**	-.37**	-.24	**-.27***	.14	.00	.15	.11	.08
Slope awake to bedtime	.07	.05	-.14	-.29*	-.09	**-.27***	-.03	-.09	.03	-.14	.07
Slope CAR to bedtime	-.11	.28*	.22	-.03	.20	-.02	-.23	-.08	-.15	-.23	-.08
AUCg	.00	-.20	-.09	.07	.02	.01	.02	.03	-.05	.19	.10
AUCi from bedtime	.03	-.29*	-.02	.13	-.02	.00	.05	-.09	-.05	.21	.09
AUCi from low value	.02	-.29*	-.04	.12	-.07	.02	.09	-.03	-.01	.26*	.15

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Appendix H Qualitative Interview Guide

In our previous visits together you have filled out some forms and questionnaires, and we've done an interview in which I had some specific questions for you. Today is going to be a little different. The purpose of the interview today is for me to get a better understanding of what your life is like overall—a bigger picture perspective of you. Would it be ok with you if I recorded today's interview so that I can remember what you said today?

Feel free to start wherever you would like…

[women typically mention a few circumstances of interest, and I ask a few general probes]
What was that like for you?
How did you handle that?
Tell me more about what you mean by…
So if I am understanding you right….
You mentioned earlier…., but you also said…[confrontation used sparingly and carefully]

[The following topics are also addressed at some point, in a way that flows with the rest of the interview]

PREGNANCY

What has this pregnancy been like for you?

Are there things you are excited about?
Are there things that have worried you?
How do you feel overall about being pregnant?
Are there things that have been hard to deal with?
In what specific ways have you tried to cope with… (the stated difficulties)?

HEALTH

How do you define health?
Are there any ways that you have thought about your health differently now that you are pregnant?
Are there any specific changes or goals you are trying to make towards your health?

CHILDHOOD

Would you describe your childhood as easy, difficult, or both?
What about your childhood made it easy or difficult?
How would you describe your relationship with your mother (or primary caregiver)?
In what ways do you want your baby's childhood to be the same as yours? Different from yours?
In what ways do you want to be like your mother/primary caregiver? Different from your mother?

MOTIVATIONAL, FUTURE-ORIENTED GOAL PLANNING

Thinking about your life right now: the place where you live, your neighborhood, your job, your income, your relationships, your health. Are there things about your life right now that you hope will be different in one year from now? Five years from now?
What are the things that you will need to do between now and then to reach those goals?
Have you made any specific plans to reach those goals?