Received: 3 September 2019 | Revised: 13 April 2020 | Accepted: 14 May 2020

DOI: 10.1002/dev.22000

RESEARCH ARTICLE

Developmental Psychobiology WILEY

Early and current life adversity: Past and present influences on maternal diurnal cortisol rhythms during pregnancy

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Funding information
Northwestern University Institute for Policy Research; U.S. Department of Education, Institute of Education Sciences, Multidisciplinary Program in Education Sciences, Grant/Award Number: R305B140042; Weinberg College of Arts and Sciences; NorthShore Research Career Development Award; NorthShore University HealthSystem Auxiliary Research Scholar Award; National Children's Study, Grant/Award Number: HHSN275201200007I—HHSN27500005

Abstract

Stress during pregnancy affects maternal health and well-being, as well as the health and well-being of the next generation, in part through the hypothalamic-pituitary-adrenal (HPA) axis. Although most studies have focused solely on proximal experiences (i.e., during the pregnancy) as sources of prenatal stress, there has been a recent surge in studies that examine maternal early life adversity as a source of stress system dysregulation during pregnancy. The current study of 178 pregnant women examined the association of economic and life stress experienced during two time periods (i.e., childhood and pregnancy) with maternal HPA axis activity during the third trimester of pregnancy. Findings indicated that a current annual income of less than $15,000 and greater childhood disadvantage were associated with a flatter diurnal cortisol slope. Childhood maltreatment, particularly sexual abuse, was associated with a higher cortisol awakening response (CAR), even when controlling for recent adversity. We found some evidence that past adversity moderates the relationship between current adversity and diurnal cortisol, specifically for economic adversity and waking cortisol. Overall, our findings indicate that early life stressors play an important and underappreciated role in shaping stress biology during pregnancy.

KEYWORDS

childhood maltreatment, diurnal cortisol rhythms, HPA axis, pregnancy, salivary cortisol, stressful life events

1 | INTRODUCTION

Exposure to psychosocial stress has implications for development, health, and well-being across the lifespan (Lupien, McEwen, Gunnar, & Heim, 2009). Considerable attention has been given to prenatal maternal stress, as stress during this period has implications for maternal health and well-being (Coussons-Read, 2013; Lobel, 1994), and for the health and well-being of the next generation (DiPietro, 2012; Van den Bergh et al., 2017). The hypothalamic-pituitary-adrenal (HPA) axis is particularly responsive to stress, and exposure to chronic or major life stress can cause diurnal cortisol patterns to become dysregulated (Adam et al., 2017). Studies have increasingly shown that adverse experiences throughout the maternal lifespan, including during the mother's own childhood, are associated with cortisol during pregnancy (Bublitz & Stroud, 2013; Khoury, Enlow, Plamondon, & Lyons-Ruth, 2019; Shea et al., 2007; Swales

et al., 2018; Thomas et al., 2018). Specifically, Bublitz and Stroud (2012) was the first study to show that women who experienced childhood trauma—specifically sexual abuse—is associated with a greater cortisol awakening response (CAR) during pregnancy, compared to women without a history of trauma/abuse.

Several recent studies have indicated that childhood stress remains predictive of cortisol during pregnancy, even when accounting for more proximal stressors (Epstein et al., 2019; Swales et al., 2018). Multiple recent studies of prenatal maternal stress (Bowers et al., 2018; Swales et al., 2018) also report a significant interaction between childhood and adult adversity on hair cortisol. These findings suggest that experiencing more childhood stress may sensitize individuals to stress in adulthood, thereby accentuating the relationship between ongoing stress and HPA axis functioning. Findings have been more mixed for studies that examine diurnal cortisol. Epstein et al. (2019) showed that the relationship between adversity in adulthood and dysregulated diurnal cortisol (i.e., a blunted CAR and steeper slope) was moderated by childhood adversity. However, Thomas et al. (2018) found no significant interactions between adverse childhood experiences (ACEs) and more proximal stressors in predicting diurnal salivary cortisol. To further contribute to this literature, we examine multiple domains of stress (economic and life stress) from two time periods across the mother's lifespan (e.g., in childhood and during pregnancy) as potential contributors to maternal stress levels and HPA axis dysregulation, as indexed by diurnal salivary cortisol, during pregnancy.

1.1 | HPA axis overview and cortisol during pregnancy

The HPA axis is one key mechanism through which stress may affect maternal and child health. Both social and physical stress activate the HPA axis, leading to a cascade of hormonal responses that culminates in the release of the glucocorticoid cortisol (McEwen, 1998). Cortisol has two primary dynamics of interest: an acute response to an immediate stressor, and a daily rhythm. The daily cortisol rhythm is characterized by moderately high levels at waking and a steep increase to a peak approximately 30 to 45 min after awakening (called the cortisol awakening response, or CAR), followed by a decline in levels throughout the day and a nadir at bedtime (Adam & Kumari, 2009; Pruessner et al., 1997). This diurnal rhythm is both affected by stress and related to health-relevant outcomes (Adam et al., 2017).

Maternal cortisol is important to consider during pregnancy because (a) HPA axis activity is dramatically altered during pregnancy and (b) cortisol is able to cross the placental barrier to affect the fetus, especially in later stages of pregnancy (Gitau, Cameron, Fisk, & Glover, 1998). Cortisol levels steadily increase throughout normative gestation, eventually peaking at the third trimester (Duthie & Reynolds, 2013). Overall, the stress response becomes dampened during pregnancy, and the CAR is attenuated in response to stress during the third trimester (Entringer, Buss, Shirtcliff, et al., 2010). The fetus is mostly protected from increasing cortisol levels by the enzyme placental 11-β hydroxysteroid dehydrogenase 2 (11β-HSD 2) (Benediktsson, Calder, Edwards, & Seckl, 1997; Duthie & Reynolds, 2013), although maternal stress (and subsequent activation of the HPA axis) has been associated with preterm birth and low birth weight (Dunkel Schetter, 2011). Moreover, these alterations in the HPA axis throughout pregnancy relate to the onset of maternal mood disorders that are increasingly prevalent postpartum (Duthie & Reynolds, 2013; Mastorakos & Ilias, 2000).

1.2 | The origins of maternal prenatal stress

Maternal cortisol levels increase two- to four-fold throughout the course of normative gestation, reaching peak levels in the third trimester (Davis & Sandman, 2010; Sandman et al., 2006). While cortisol plays a necessary role for development in utero, deleterious effects arise when maternal stress levels are too high (Nepomnaschy et al., 2006). Elevated maternal stress during pregnancy has been linked to pre-term delivery and low birth weight infants (Davis & Sandman, 2010; Sandman et al., 2006), as well as negative outcomes in the offspring, including dysregulated stress system functioning (Davis, Glynn, Waffarn, & Sandman, 2011); altered fetal brain development (Moog et al., 2018); worse cognitive functioning (Davis & Sandman, 2010); and worse physical and mental health (Beydoun & Saftlas, 2008).

Findings suggest that, similar to other times across the life course, proximal stressors influence maternal cortisol patterns during pregnancy. A recent metaanalysis found a small but significant relationship between greater life adversity and increased hair cortisol levels (Khoury et al., 2019). During pregnancy, an increase in stressful experiences is associated with increased HPA activation, in addition to adverse birth outcomes (Behrman & Butler, 2007). There is some evidence that pregnant women who report a greater number of stressful life events have elevated cortisol levels in later pregnancy, but not in early pregnancy (Obel et al., 2005); however, these findings are mixed. Deuschle et al. (2018) found that higher glucocorticoid levels in amniotic fluid were associated with lower family income during pregnancy, but not with maternal adverse childhood events. Notably, the authors did not assess economic disadvantage during childhood in this study. In the first study of childhood economic disadvantage and hair cortisol, Bosquet Enlow et al. (2019) found that economic disadvantage during both childhood and pregnancy was associated with greater hair cortisol levels, and that the relationship between childhood disadvantage and cortisol was mediated by economic adversity during pregnancy.

There is growing evidence that early life maternal stressors also shape prenatal HPA axis functioning, specifically through cortisol. Childhood maltreatment and adversity are especially potent predictors of HPA axis dysregulation during pregnancy. Shea et al. (2007) found that greater experiences of childhood maltreatment were associated with lower baseline cortisol levels. They also examined current depression levels, which were no longer associated with

a blunted CAR when accounting for antidepressant medication. Women who reported childhood sexual abuse exhibited higher CARs during pregnancy than those who experience non-sexual trauma, or no trauma (Bublitz & Stroud, 2013). Another recent study found that maternal Adverse Childhood Experience (ACE) scores were associated with a higher CAR when accounting for adult stress levels (Thomas et al., 2018).[1] Importantly, these studies did not measure financial stress in childhood, despite findings that early economic disadvantage has lasting health consequences throughout the lifespan (e.g., faster epigenetic aging, Austin et al., 2018; adverse pregnancy outcomes, Miller et al., 2017).

In light of findings that past and recent stressors matter for HPA axis functioning, the interaction between childhood and adult adversity has garnered more attention in recent work on prenatal maternal stress. Swales et al. (2018) reported a significant interaction between childhood and adult stressors in predicting hair cortisol levels during pregnancy, which suggests that experiencing childhood adversity may sensitize individuals to stress in adulthood. Epstein et al. (2019) found that greater childhood adversity was associated with an elevated CAR during pregnancy, and that childhood adversity moderated the relationship between HPA axis functioning and stress and depression in adulthood, such that adult adversity only predicted a blunted CAR and steeper slope for women with a past history of childhood adversity. Greater depression was associated with a flatter slope, but only for those with a past history of adversity. These findings suggest the need to consider the role of maternal early life stress, in addition to current stress, in shaping a pregnant woman's biological stress response, which can in turn have developmental consequences for her offspring.

1.3 | Current study

Prior research has tended to focus on stress within one developmental period, without accounting for other periods of the lifespan, or within one domain of stress, without respect to other stress domains. Investigating the relative contributions of different types of stress from different life periods may be especially informative. While some studies have used this approach (Deuschle et al., 2018; Gray, Jones, Theall, Glackin, & Drury, 2017; Thomas et al., 2018; Wolitzky-Taylor et al., 2017), no study to our knowledge has examined multiple stress domains across the lifespan and their respective associations with diurnal cortisol during pregnancy. Prior work has generally focused on investigating HPA axis functioning during pregnancy as a potential mechanism for transmitting early life adversity to offspring (Thomas et al., 2018), or examining the interaction between childhood adversity and proximal stressors (Epstein et al., 2019). We build on this research to examine the influence of economic disadvantage and other types of life stress (i.e., childhood maltreatment and stressful life events in adulthood) during both childhood and pregnancy on the diurnal cortisol rhythms of pregnant women. We expected adversity in adulthood to be associated with diurnal cortisol. We further expected financial and social adversity in early life to be significantly related to the diurnal rhythm, even when accounting for more proximal stressors in adulthood. In follow-up analyses, we conducted specificity analyses to determine which facets of childhood maltreatment were associated with diurnal cortisol. Based on prior research (Bublitz & Stroud, 2012), we anticipated that sexual abuse would be related to dysregulated diurnal cortisol. We also examined the interactions between childhood and adulthood adversity, expecting that greater adversity during childhood would moderate adult adversity to predict dysregulated diurnal cortisol (Epstein et al., 2019).

2 | MATERIALS AND METHODS

2.1 | Design and overview

Data for these analyses came from the Measurement of Maternal Stress (MOMS) study, which collected stress and health data from 744 pregnant women across four US sites (for more information see: Ross et al., 2016). During their first study visit (second trimester), participants completed a questionnaire with demographic and psychosocial stress questions. At this time, a subsample of participants from the Pittsburgh, PA study site (N = 200) was recruited to provide physiological measures, including salivary cortisol, over four days in order to assess their HPA functioning. During the second visit, which took place during the third trimester, participants completed a questionnaire that probed their recent life stress.

2.2 | Participants

Participants were recruited between 2013 and 2015, and were assessed during the second trimester (between 12 and 20 and 6/7 weeks' gestation) and again during the third trimester (between 32 and 35 and 6/7 weeks' gestation). For inclusion in the study, women were required to be (a) 18 years or older with (b) a singleton intrauterine pregnancy, (c) less than 21 weeks pregnant at their first assessment, and (d) English speaking.[2]

2.3 | Salivary cortisol

Cortisol diurnal rhythms were assessed in a sub-sample of participants. At their second trimester visit, participants received supplies to collect salivary samples for the subsequent four days. Participants were asked to provide six saliva samples on each day of the four-day sequence to model the distinct circadian rhythm exhibited by cortisol. Samples were scheduled to be collected: immediately upon awakening; 30 min after awakening; 60 min after waking; 12p.m.; 4p.m.; 8p.m.; and at bedtime. Participants placed the collection tubes in the refrigerator until they returned the entire set to the laboratory the day after all samples were collected. In the laboratory, the samples were centrifuged and then frozen and subsequently assayed

for cortisol using a high-sensitive enzyme-immunoassay (Salimetrics, PA). Salivary cortisol analyses were conducted at the University of California, Irvine. The average intra-assay CV was 4.64% and the inter-assay CV was 3.32%. From the original sample, 15% of cortisol data were missing. In order to have sufficient data to appropriately model diurnal cortisol rhythms, participants were included in analyses if they (a) provided at least six saliva samples across the four days and (b) had at least one day where they had collected both the morning and evening saliva samples. These criteria excluded 12 participants from the analytic sample and reduced missing cortisol samples to 11%.

2.4 | Questionnaires

Childhood maltreatment was assessed using the childhood trauma questionnaire (CTQ; Bernstein et al., 1994), a 28-item retrospective measure of child abuse and neglect experienced between ages 0–17. Participants responded to items using a Likert scale from 1 = *Never True* to 5 = *Always True*, or opted out of responding by answering *Do Not Know/Refuse*. The CTQ assesses multiple dimensions of trauma using five subscales (i.e., emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect). Low-moderate and moderate-severe maltreatment scores were calculated using guidelines in the CTQ scoring manual, which provides a moderate cutoff point that varies by scale (emotional abuse ≥ 13; physical abuse ≥ 10; sexual abuse ≥ 8; emotional neglect ≥ 15; and physical neglect ≥ 10). The moderate/severe maltreatment group included anyone who scored above the moderate cutoff in any category, whereas the low/moderate maltreatment group included anyone who scored below the moderate cutoff in any category (but not no maltreatment), but also did not have any moderate/severe maltreatment. The reference group was comprised of the women who experienced no childhood maltreatment. For the follow-up analyses, we created dichotomous variables for each of the five subscales to indicate whether they had experienced any of the facets of childhood maltreatment. A score of 0 indicated that there was no childhood maltreatment in that category, while a score of 1 indicated the presence of childhood maltreatment, combining the low/moderate and moderate/severe categories.

Childhood economic disadvantage (Miller, Brody, Yu, & Chen, 2014) was measured by asking participants a series of questions about their family's economic conditions between ages 0–16. The eight-item scale asked, for example, whether their family owned a home, could obtain medical treatment when necessary, received public assistance, or owned a television. One point was given for each instance of disadvantage, and the items were summed to create a total sum score for childhood disadvantage.

Current life stress was assessed by the Stressful Life Events Schedule (SLES; Williamson et al., 2003), an in-depth interview that asks participants about the occurrence of 91 stressful events in the 12 months prior to the interview. There are nine main categories of events: crime, deaths, education, health, housing, money, romantic relationships, other relationships, and work. Our analyses used a total score that summed all stressful events in that year. A panel of trained reviewers determined the threat level of a stressful event (e.g., severe/not severe) on a four-point scale, based on contextual and biographical information. Linear dissipation modeling was used to create total scores based on these objective ratings. The SLES was administered during the third trimester visit.

Participants categorically reported their current income within five categories: less than $15,000, $15,000–$29,999, $30,000–$49,999, $50,000–$100,000, and over $100,000. Based on the distribution of responses, we collapsed income into four groupings: <$15,000, $15,000–$49,999, $50,000–$100,000, and >$100,000. The highest income group (>$100,000) was used as the reference group in all analyses.

2.5 | Covariates

To account for possible confounders (other maternal characteristics previously associated with the diurnal cortisol rhythm and also potentially associated with maternal SES and life stress), we considered maternal age (years), self-reported maternal race, body mass index (BMI; kg/m^2), smoking status, marital status, parity, and gestational age at time of cortisol collection. Self-identified race was included using three dummy variables, coded as non-Hispanic white, black, and other race (including Hispanics). The non-Hispanic white group was the reference group in all analyses. Smoking status was coded as "yes" = 1/"no" = 0 based on whether mothers reported being current smokers.

2.6 | Other variables

Depression, perceived stress, and prenatal distress were not significantly related to diurnal cortisol, and were thus not included as covariates in our final models. Depression was measured by the 20-item Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977), perceived stress was measured by the 10-item Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983), and prenatal distress was measured by the 12-item prenatal distress questionnaire (PDQ; Yali & Lobel, 1999).[3]

2.7 | Analysis Plan

In our analysis, we used three-level hierarchical linear models to examine both within- and between-individual variation in diurnal cortisol rhythms. This method is recommended as a best practice for analyzing diurnal cortisol rhythms (Adam, 2006; Adam et al., 2015; Hruschka, Kohrt, & Worthman, 2005) as it accounts for the non-independence resulting from the nested data structure of the cortisol

data (i.e., momentary cortisol samples nested within days nested within individuals) (Raudenbush, Bryk, & Congdon, 2002). In these models, Level 1 represents each of the six daily samples, Level 2 represents the day, and Level 3 is the person-level. At Level 1, we regressed the time of day for each sample (entered into the model as time since waking) on each individual's total cortisol. Cortisol values were natural log transformed prior to analysis in order to normalize the data (Adam & Kumari, 2009). This approach models the general decline of cortisol observed over each day. We also entered in a quadratic term (the square of time since waking) at Level 1 to account for the general slowing of the daily decline in cortisol. Time was centered at waking (e.g., waking time = 0), which allows us to interpret the intercept as an individual's wake-time cortisol. We modeled the cortisol awakening response (CAR) by adding a dummy variable to indicate the sample taken at both 30 min after waking (time 2 = 1, all other times = 0) and 60 min after waking (time 3 = 1, all other times = 0). For Level 2, we included daily wake time (hours). At Level 3, we added in the individual-level covariates as described above. Before imputation, 77.3% of participants had complete data for predictor and control variables. We used multiple imputation procedures in SAS using 20 imputations to generate estimates of values for missing data.

Using this general model, we examined two sets of individual level (Level 3) characteristics. In the first model (Current Stress Only Model), we added the SLES composite and income predictors to account for current stress and disadvantage. We also included interactions of these terms with the timing of the sample and the quadratic timing term, in order to model associations between stress and income predictors and the slope of the diurnal cortisol rhythm. We also included an interaction of each income group with the CAR (30 and 60 min) to examine whether income was significantly associated with the CAR. In the second model (Current and Childhood Stress Model), we used the same predictors but also added in the childhood maltreatment and disadvantage at Level 3. We also included interaction terms for these childhood stressors with time since waking, and childhood maltreatment with the CAR (30 and 60 min). This model assessed whether recent stressful events and socioeconomic status remained significant after accounting for childhood experiences of maltreatment and disadvantage, and likewise, whether childhood experiences predicted maternal prenatal cortisol above and beyond their current stress levels.

We also conducted several follow-up analyses. First, we considered whether specific facets of childhood maltreatment were associated with diurnal cortisol. We conducted multilevel models with each subscale as an independent predictor of diurnal cortisol, re-running all models to account for proximal stressors. We also conducted interaction analyses with prior and recent adversity predicting diurnal cortisol in order to determine whether the associations were potentiated by one another. Separate models were run for (a) economic disadvantage in childhood and adulthood and (b) childhood maltreatment and adult life stress. Our analyses were conducted in SAS version 9.3.

TABLE 1 Descriptive statistics of women in the sample

	M (*SD*) or %	Minimum	Maximum
Age (years)	30.12 (5.06)	19.7	44.7
BMI (kg/m^2)	28.13 (7.48)	18.8	60.2
Current smoker	6.2.0%	0	1
Race			
White	80.9%	0	1
Black	16.3%	0	1
Other race	2.8%	0	1
Perceived Stress Scale	15.17 (6.09)	2.0	32.0
Maternal depression	12.47 (9.10)	0.0	58.0
Prenatal distress	14.06 (7.18)	0.0	38.0
Income (USD)	15.17 (6.09)	2.0	32.0
<$15,000	12.6%	0	1
$15,000–49,999	26.4%	0	1
$50,000–99,999	37.9%	0	1
≥$100,000	23.0%	0	1
Married	83.7%	0	1
Nulliparous	44.4%	0	1
Gestational age at visit (weeks)	16.10 (2.39)	10	20
Current SLES	43.6 (42.07)	0	307.5
Childhood SES disadvantage	1.04 (1.28)	0	6
Childhood maltreatment			
Low/moderate	27%	0	1
Moderate/high	40%	0	1

Abbreviations: BMI, body mass index; SLES, stressful life events schedule; SES, socioeconomic status.

3 | RESULTS

3.1 | Descriptive information

Table 1 presents descriptive statistics for our sample (*N* = 178). Participants were expectant women an average of nearly 30 years of age (*SD* = 5.1). The majority (81%) identified as non-Hispanic white, with 16% identifying as black and the remaining 3% as other race. Participants had relatively higher income in comparison to the United States population, with 60% reporting an income of over $50,000. They reported low to moderate levels of depression (*M* = 12.47, *SD* = 9.10), with 76% of the sample scoring below 16, which is widely considered to be the clinical threshold for depression. They also reported moderate levels of perceived stress (*M* = 15.17, *SD* = 6.09) and prenatal distress (*M* = 14.06, *SD* = 7.18).

Associations between the four key predictor variables are presented in Table 2. Higher current income was associated with less childhood maltreatment and economic disadvantage, but not with

TABLE 2 Intercorrelations between key predictor variables

	1.	2.	3.	4.
1. Current income	—			
2. Current SLES	−0.11	—		
3. Childhood disadvantage	−0.42**	0.07	—	
4. Childhood maltreatment	−0.33**	0.32**	0.31**	—

**$p < .01$.

levels of current life stress. Childhood maltreatment was significantly correlated with greater childhood disadvantage and current life stress. Childhood disadvantage and current life stress were not significantly associated. All significant correlations were low to moderate (ranging from 0.31 to 0.42), such that it was reasonable to test whether each of these variables makes independent contributions to the prediction of maternal prenatal diurnal cortisol.

3.2 | Diurnal cortisol rhythm

3.2.1 | General rhythm

Consistent with prior research, cortisol levels were highest in the morning, with levels significantly declining, on average, by 17% per hour (at waking) (Table 3, Model 1). This descent decelerated across the day by 0.5% per hour starting at waking, as indicated by a significant and positive quadratic term ($Time^2$). On top of this underlying diurnal rhythm, cortisol surged by 15% in the first 30 min after waking. By 60 min after awakening, cortisol had declined from its peak but was still elevated by about 5%.

3.2.2 | Covariate effects

Waking cortisol levels were significantly higher for women who smoked, were married or cohabitating, and were further along in their pregnancy, and significantly lower for women who were older, had a higher BMI, were multiparous, and who were black (as compared to non-Hispanic white). There were no significant differences in waking cortisol by Hispanic race-ethnicity, nor were there differences for slope by race-ethnicity. The CAR at 30 and 60 min was significantly lower for individuals who woke later.

3.3 | Current stress and cortisol

We next examined whether the diurnal rhythm was influenced by current economic and life stress, as measured by current income and current life stress (SLES) (Table 2, Model 1). Waking levels were not significantly associated with life stress or income levels. Only current income was associated with differences in cortisol slope. Specifically, the decline in cortisol levels across the day was significantly flatter among those making <$15,000 ($b = 0.09$, $SE = 0.03$, $p = .004$), in comparison to those making $100,000 or more per year. Neither life stress nor income was associated with the CAR.

3.4 | Current stress, childhood adversity, and cortisol

Next, we examined whether measures of childhood disadvantage and maltreatment were significant over and above current disadvantage and life stress, and whether the observed associations between current economic and social stress and cortisol were attenuated by including measures of childhood disadvantage and maltreatment. Full regression results are presented in Table 3, Model 2.

3.4.1 | Stress during pregnancy

After controlling for childhood maltreatment and economic disadvantage, individuals making <$15,000 still had significantly flatter diurnal slopes ($b = 0.09$, $SE = 0.03$, $p = .004$). There were no significant associations between life stress and diurnal cortisol.

3.4.2 | Childhood adversity

After controlling for current income and life stress, greater childhood economic disadvantage was associated with a flatter cortisol slope ($b = 0.02$, $SE = 0.007$, $p = .01$). Greater economic disadvantage was also associated with less deceleration of this decline, as indicated by an interaction with the quadratic time term ($b = -0.002$, $SE = 0.0006$, $p < .01$). Conversely, childhood maltreatment was not significantly associated with the diurnal slope.

Individuals who experienced moderate/severe childhood maltreatment did, however, have a significantly greater CAR, with higher concentrations of cortisol at both 30 ($b = 0.14$, $SE = 0.07$, $p = .04$) and 60 min after awakening ($b = 0.20$, $SE = 0.08$, $p = .01$) than individuals with no or low-to-moderate levels of maltreatment. These findings for childhood disadvantage and childhood maltreatment were significant, controlling for current demographics (including income) and levels of recent life stress.

Childhood maltreatment specificity analyses

Next, we examined the relationship between specific types of childhood maltreatment and diurnal cortisol (See Table 4). Sexual abuse was significantly associated with an elevated CAR (30-min CAR: $b = 0.18$, $SE = 0.06$, $p = .005$; 60-min CAR: $b = 0.22$, $SE = 0.06$, $p < .001$), which remained stable when controlling for proximal stressors. There were trending associations between physical neglect and flatter diurnal slope ($b = 0.04$, $SE = 0.02$, $p = .07$), as well as between emotional abuse and a greater CAR ($b = 0.10$, $SE = 0.05$, $p = .06$), though these findings became non-significant when accounting for

TABLE 3 Multilevel models of the associations between (a) current stress (adulthood) and cortisol and (b) current stress, childhood stress, and cortisol

	MODEL 1			MODEL 2		
	Coefficient[a]	SE	*p*-value	Coefficient[a]	SE	*p*-value
Intercept, γ_{000}	−1.61	0.11	<.0001	−1.60	0.11	<.0001
Time	−0.17	0.02	<.0001	−0.17	0.02	<.0001
Time^2	0.005	0.001	<.001	0.005	0.001	<.001
CAR30	0.15	0.07	.03	0.15	0.07	.03
CAR60	0.05	0.07	.47	0.05	0.07	.47
Current smoker	0.21	0.05	<.0001	0.20	0.05	<.0001
Married	0.08	0.03	.02	0.08	0.03	.02
Gestational age	0.03	0.004	<.0001	0.03	0.004	<.0001
Parity	−0.03	0.01	<.0001	−0.03	0.01	.02
Black	−0.20	0.07	.01	−0.19	0.08	.01
Other race	−0.04	0.08	.55	−0.03	0.07	.67
Time × Black	0.013	0.01	.01	0.01	0.01	.43
Time × Other	−0.013	0.01	.48	−0.01	0.01	.21
Age (years)	−0.008	0.003	.001	−0.01	0.01	.001
BMI (kg/m^2)	−0.01	0.001	<.0001	−0.01	0.001	<.001
<$15,000	−0.09	0.09	.29	−0.09	0.09	.29
$15,000–49,999	−0.12	0.06	.05	−0.12	0.06	.05
$50,000–100,000	−0.005	0.05	.92	−0.01	0.05	.86
Time × <$15,000	0.09	0.03	.004	0.09	0.03	.004
Time × $15–49,999	0.04	0.02	.13	0.04	0.02	.13
Time × $50–99,999	0.03	0.02	.21	0.03	0.02	.21
Time^2 × <$15,000	−0.005	0.002	.03	−0.005	0.002	.03
Time^2 × $15–49,999	−0.002	0.002	.18	−0.002	0.002	.18
Time^2 × $50–99,999	−0.002	0.002	.22	−0.002	0.002	.22
CAR30 × Wake time (hrs)	−0.04	0.02	.03	−0.04	0.02	.03
CAR60 × Wake time (hrs)	−0.06	0.02	.002	−0.06	0.02	.002
CAR30 × <$15,000	0.11	0.11	.30	0.11	0.11	.30
CAR30 × $15–49,999	0.06	0.08	.49	0.06	0.08	.50
CAR30 × $50–99,999	0.03	0.08	.72	0.03	0.08	.70
CAR60 × <$15,000	0.12	0.11	.30	0.13	0.11	.30
CAR60 × $15–49,999	−0.01	0.09	.91	−0.01	0.09	.91
CAR60 × $50–99,999	0.02	0.08	.80	0.02	0.08	.80
SLES	−0.001	0.001	.17	−0.001	0.001	.17
Time × SLES	0.0001	0.0003	.93	0.0001	0.0003	.93
ChDis				−0.002	0.02	.92
Time × ChDis				0.02	0.01	.03
Time^2 × ChDis				−0.001	0.001	.02
ChMal—low/mod				−0.06	0.05	.23
ChMal—mod/sev				0.04	0.05	.44
Time × ChMal—low/mod				0.006	0.02	.76
Time × ChMal—mod/sev				0.002	0.02	.97

(Continues)

TABLE 3 (Continued)

	MODEL 1			MODEL 2		
	Coefficient[a]	SE	*p*-value	Coefficient[a]	SE	*p*-value
CAR30 × ChMal—low/mod				0.11	0.07	.14
CAR30 × ChMal—mod/sev				0.14	0.07	.04
CAR60 × ChMal—low/mod				0.09	0.08	.18
CAR60 × ChMal—mod/sev				0.20	0.08	.01

Abbreviations: BMI, body mass index; CAR30, Cortisol awakening response, measured at 30 min; CAR60, Cortisol awakening response, measured at 60 min; ChDis, childhood disadvantage; ChMal, childhood maltreatment; SLES, stressful life events schedule.

[a]Units represent the natural log of salivary cortisol, measured in mg/dL.

proximal stressors. Physical abuse and emotional neglect were not significantly related to diurnal cortisol (*p*s > .05).

3.4.3 | Interactions between childhood and adult stress

Childhood maltreatment and current life stress

There were no significant associations between the interaction of childhood maltreatment and current life stress with waking levels of cortisol, the diurnal slope, or the CAR (See Table 5, Model 1).

Childhood and current economic disadvantage

There were no significant associations between the interaction of childhood and current economic disadvantage with the diurnal slope or the CAR (See Table 5, Model 2). However, the interaction between childhood disadvantage and current income was significantly associated with waking cortisol levels for those with an income between $15,000 and $100,000, such that greater early economic disadvantage and lower income during pregnancy predicted lower waking cortisol levels ($15,000–$49,900: $b = -0.16$, $SE = 0.09$, $p = .04$; $50,000–$100,000: $b = -0.22$, $SE = 0.08$, $p = .01$). Childhood disadvantage and current income of <$15,000 was marginally associated with lower waking cortisol levels ($b = -0.17$, $SE = 0.09$, $p = .06$).

4 | DISCUSSION

The present study examined associations between early life and recent adversity and HPA axis functioning during pregnancy. Our results indicated that childhood maltreatment, childhood economic disadvantage, and current economic disadvantage were all associated with HPA axis functioning, such that moderate/severe childhood maltreatment was associated with a higher CAR, while childhood economic disadvantage and lower current income were associated with a flatter diurnal cortisol slope. Of the specific dimensions of childhood maltreatment, only experiencing sexual abuse in childhood was associated with a heightened CAR. Our results also showed that experiencing early economic adversity accentuated the relationship between current economic adversity and lower waking cortisol levels. No other significant interactions between prior and recent adversity emerged.

We found that childhood maltreatment is associated with a larger CAR, which is in line with several studies that have shown that early life adversity predicts the CAR (Bosquet Enlow et al., 2019; Bublitz & Stroud, 2012; Thomas et al., 2018). Similar to Bosquet Enlow et al. (2019), we found that economic adversity in both childhood and pregnancy was related to dysregulated HPA axis functioning, showing convergence across cortisol indicators (e.g., hair and salivary cortisol).

This study furthers our understanding of the lifelong, intergenerational effects of developmental (e.g., childhood) stress on the HPA axis even when controlling for current maternal adversity. Considering multiple time frames (Gunnar & Adam, 2012), in addition to probing domain specificity, is an innovative approach to studying psychosocial and biological stress, particularly during pregnancy. By examining the types and timings of stressors that are most likely to "get under the skin," we are better able to understand appropriate time points for intervention. Our findings are in line with a burgeoning literature that examines the contributions of stress from multiple developmental periods (and across multiple domains) to compare the relative contribution of each (Gray et al., 2017; Kessler et al., 2019; Swales et al., 2018; Thomas et al., 2018; Vrshek-Schallhorn et al., 2014; Wolitzky-Taylor et al., 2017).

The literature on the interactions between prior and recent stress is mixed, with some cortisol studies showing that proximal stress moderates the relationship between early life stress and diurnal cortisol (Bublitz & Stroud, 2013; Epstein et al., 2019), and others finding no significant associations between early life stress and proximal stressors in predicting cortisol (Thomas et al., 2018). Our results revealed a significant interaction between childhood economic disadvantage and current income to predict lower waking cortisol levels, suggesting that early economic adversity moderated proximal economic stress for one indicator of diurnal cortisol. Extant

TABLE 4 Multilevel models of the associations between childhood maltreatment subscales and diurnal cortisol

	Sexual abuse		Physical neglect		Physical abuse		Emotional neglect		Emotional abuse	
	Coefficient[a] (SE)	*p*-value	Coefficient[a] (SE)	*p*-value	Coefficient[a] (SE)	*p*-value	Coefficient[a] (SE)	*p*-value	Coefficient[a] (SE)	*p*-value
Intercept, γ_{000}	−1.60 (0.12)	.001	−1.61 (0.12)	.001	−1.62 (0.12)	.001	−1.63 (0.12)	.001	−1.60 (0.12)	.001
Time	−0.17 (0.01)	<.001	−0.11 (0.01)	<.001	−0.17 (0.01)	<.001	−0.17 (0.01)	<.001	−0.17 (0.01)	<.001
Time^2	0.004 (0.001)	<.0001	0.003 (0.001)	<.0001	0.003 (0.001)	<.0001	0.003 (0.001)	<.0001	0.003 (0.001)	<.0001
CAR30	0.21 (0.03)	<.0001	0.25 (0.03)	<.0001	0.24 (0.03)	<.0001	0.25 (0.03)	<.0001	0.21 (0.03)	<.0001
CAR60	0.11 (0.03)	<.0001	0.14 (0.03)	<.0001	0.15 (0.03)	<.0001	0.15 (0.03)	<.0001	0.13 (0.03)	<.0001
Current Smoker	0.19 (0.07)	.005	0.18 (0.07)	.007	0.18 (0.07)	.008	0.19 (0.07)	.005	0.19 (0.07)	.005
Married	0.02 (0.05)	.73	0.02 (0.04)	.67	0.02 (0.05)	.65	0.02 (0.05)	.73	0.01 (0.05)	.76
Gestational Age	0.03 (0.007)	<.0001	0.03 (0.01)	<.0001	0.03 (0.01)	<.0001	0.03 (0.01)	<.0001	0.03 (0.01)	<.0001
Parity	−0.02 (0.02)	.24	−0.02 (0.02)	.16	−0.02 (0.02)	.23	−0.03 (0.02)	.13	−0.02 (0.02)	.21
Race	−0.22 (0.06)	<.0001	−0.22 (0.06)	<.0001	−0.22 (0.06)	<.0001	−0.21 (0.06)	.0002	−0.22 (0.06)	<.0001
Other Race	0.06 (0.10)	.57	0.06 (0.10)	.45	0.04 (0.10)	.69	0.03 (0.10)	.77	0.06 (0.10)	.54
Maternal Age	−0.004 (0.004)	.19	−0.004 (0.003)	.27	−0.005 (0.004)	.16	−0.005 (0.004)	.21	−0.005 (0.004)	.20
BMI	−0.01 (0.002)	<.0001	−0.01 (0.002)	<.0001	−0.01 (0.002)	<.0001	−0.01 (0.002)	<.0001	−0.01 (0.002)	<.0001
Waking cortisol	−0.08 (0.06)	.14	−0.004 (0.07)	.95	0.03 (0.06)	.64	0.07 (0.05)	.15	−0.034 (0.05)	.46
Slope	0.03 (0.02)	.15	0.04 (0.02)	.07	0.02 (0.02)	.19	0.01 (0.02)	.50	0.02 (0.01)	.21
Slope^2	−0.002 (0.001)	.13	−0.002 (0.002)	.21	−0.002 (0.001)	.26	−0.002 (0.001)	.14	−0.001 (0.001)	.33
CAR30	0.18 (0.06)	.005	−0.01 (0.07)	.90	0.05 (0.06)	.47	−0.01 (0.06)	.87	0.10 (0.05)	.06
CAR60	0.22(0.06)	.001	0.07 (0.08)	.37	−0.02 (0.06)	.81	0.003 (0.06)	.96	0.07 (0.05)	.17

TABLE 5 Multilevel models of the associations between (a) interactions between current life stress (adulthood) and childhood maltreatment predicting cortisol and (b) interactions between current economic stress and childhood economic disadvantage predicting cortisol

	MODEL 1			MODEL 2		
	Coefficient[a]	SE	*p*-value	Coefficient[a]	SE	*p*-value
Intercept, γ_{000}	−1.61	0.11	<.0001	−1.61	0.11	<.0001
Time	−0.18	0.03	<.0001	−0.18	0.03	<.0001
Time^2	0.005	0.002	.004	0.005	0.002	.004
CAR30	0.17	0.08	.03	0.17	0.08	.03
CAR60	0.06	0.09	.51	0.06	0.09	.51
Current smoker	0.19	0.05	.002	0.19	0.05	.002
Married	0.11	0.03	<.001	0.11	0.03	<.001
Gestational age	0.03	0.004	<.0001	0.03	0.004	<.0001
Parity	−0.05	0.01	<.0001	−0.05	0.01	<.0001
Black	−0.13	0.07	.10	−0.13	0.08	.10
Other race	−0.003	0.08	.97	0.001	0.14	.97
Time × black	0.01	0.01	.48	0.01	0.01	.48
Time × Other	−0.02	0.01	.15	−0.02	0.01	.15
Age (years)	−0.01	0.003	.001	−0.01	0.003	.001
BMI (kg/m^2)	−0.01	0.001	<.0001	−0.01	0.001	<.0001
<$15,000				−0.14	0.10	.17
$15,000–49,999				−0.17	0.07	.02
$50,000–100,000				−0.10	0.07	.17
Time × <$15,000				0.11	0.03	.002
Time × $15–49,999				0.04	0.03	.09
Time × $50–99,999				0.04	0.02	.11
Time^2 × <$15,000				−0.006	0.003	.02
Time^2 × $15–49,999				−0.003	0.002	.26
Time^2 × $50–99,999				−0.002	0.002	.27
CAR30 × wake time (hrs)	−0.04	0.02	.06	−0.04	0.02	.06
CAR60 × wake time (hrs)	−0.07	0.03	.001	−0.07	0.03	.001
CAR30 × <$15,000				0.08	0.13	.52
CAR30 × $15–49,999				0.04	0.09	.63
CAR30 × $50–99,999				0.03	0.09	.73
CAR60 × <$15,000				0.10	0.13	.45
CAR60 × $15–49,999				−0.01	0.10	.91
CAR60 × $50–99,999				0.04	0.10	.67
SLES	−0.003	0.002	.07			
Time × SLES	0.001	0.001	.22			
ChDis				0.16	0.08	.04
Time × ChDis				−0.02	0.03	.56
Time^2 × ChDis				−0.001	0.002	.70
ChMal — low/mod	−0.06	0.05	.26			
ChMal — mod/sev	0.03	0.05	.62			
Time × ChMal — low/mod	0.002	0.02	.91			
Time × ChMal — mod/sev	0.001	0.02	.98			
CAR30 × ChMal — low/mod	0.11	0.08	.15			

(Continues)

TABLE 5 (Continued)

	MODEL 1			MODEL 2		
	Coefficient[a]	SE	*p*-value	Coefficient[a]	SE	*p*-value
CAR30 × ChMal — mod/sev	0.14	0.07	.04			
CAR60 × ChMal — low/mod	0.10	0.08	.23			
CAR60 × ChMal —mod/sev	0.22	0.08	.005			
SLES × ChMal — low/mod	0.003	0.002	.29			
SLES × ChMal — mod/sev	0.003	0.002	.14			
Time × SLES × ChMal — low/mod	−0.001	0.001	.44			
Time × SLES × ChMal — mod/sev	−0.001	0.001	.12			
CAR30 × SLES × ChMal — low/mod	0.001	0.004	.83			
CAR30 × SLES × ChMal —mod/sev	0.0005	0.003	.86			
CAR60 × SLES × ChMal — low/mod	0.002	0.004	.65			
CAR60 × SLES × ChMal — mod/sev	−0.003	0.003	.34			
ChDis × <$15,000				−0.17	0.09	.06
ChDis × $15,000–49,999				−0.16	0.09	.04
ChDis × $50,000–100,000				−0.22	0.08	.01
Time × ChDis × <$15,000				0.03	0.03	.34
Time × ChDis × $15,000–49,999				0.05	0.03	.08
Time × ChDis × $50,000–100,000				0.03	0.03	.29
CAR30 × ChDis × <$15,000				−0.05	0.11	.68
CAR30 × ChDis × $15,000–49,999				−0.09	0.10	.41
CAR30 × ChDis × $50,000–100,000				0.01	0.11	.90
CAR60 × ChDis × <$15,000				0.05	0.11	.62
CAR60 × ChDis × $15,000–49,999				−0.05	0.11	.65
CAR60 × ChDis × $15,000–49,999				0.06	0.11	.60

Abbreviations: BMI, body mass index; SLES, stressful life events schedule; CAR30, Cortisol awakening response, measured at 30 min; CAR60, Cortisol awakening response, measured at 60 min; ChDis, Childhood Disadvantage; ChMal, Childhood maltreatment.

[a]Units represent the natural log of salivary cortisol, measured in mg/dL.

literature supports a sensitization model of early life adversity and recent life stress on diurnal cortisol later on (Lupien et al., 2009; McEwen, 1998; Young et al., 2019), with early economic disadvantage as a particularly potent predictor of later health and well-being (Chen & Miller, 2013). Perhaps surprisingly, we did not see robust significant interactions between prior and recent life stress in predicting diurnal cortisol. However, these findings converge with a recent study that found that the association between proximal life stressors and diurnal cortisol was not moderated by adverse childhood experience (Thomas et al., 2018). These interaction findings underscore the importance of considering various types of childhood stressors, especially economic adversity, not only on their own but also in interaction with proximal stress, as they may differentially prime stress sensitivity later on.

We observed different patterns of associations of between economic disadvantage and childhood maltreatment, suggesting different pathways through which these experiences may influence different health outcomes. Economic stress experienced both earlier in life and more recently was associated with a flattened diurnal slope. Flatter cortisol slopes may be an indicator of chronic stress, and are associated with a wide range of adverse health outcomes (e.g., inflammation, obesity, depression, etc.; Adam et al., 2017).

Interestingly, moderate-to-severe childhood maltreatment was associated with a higher CAR, but was not related to the diurnal slope. Experiencing sexual abuse was especially predictive of an elevated CAR. The CAR has been prospectively associated with mood disruptions, particularly with greater risk for depression (Adam et al., 2010; Vrshek-Schallhorn et al., 2013). A higher 60-min CAR is especially interesting, as it implies either a delayed onset of the CAR or impaired recovery from the initial surge in cortisol levels.

The current study also contributes to the existing literature that highlights the particular importance of early life stress and adversity for prenatal stress biology. Our findings show that women carry early life adversities, as well as more proximal economic stressors, with them into pregnancy. This finding is consistent with other work indicating the long-lasting link between early life stress and a range of health-related outcomes across the lifespan (for example, birth outcomes, Gilles et al., 2018; Miller et al., 2017; and health disparities, Shonkoff, Boyce, & McEwen, 2009).

There are mixed findings on whether more proximal or distal factors have a greater impact on health and biological functioning (Doane et al., 2013; Kessler et al., 2019; Miller, Chen, & Zhou, 2007). Recent studies examining associations of life stress with cortisol suggest major early life experiences continue to influence the diurnal rhythm well into the future, and above and beyond current life stress (Thomas et al., 2018). Our findings are in line with these studies, suggesting that experiences of adversity and maltreatment in childhood are robustly linked to dysregulated HPA axis functioning. Also consistent with previous research, we found that current economic disadvantage was associated with cortisol (Bosquet Enlow et al., 2019; Deuschle et al., 2018), with a flatter slope observed for those in the lowest income group (Thomas et al., 2018). We extend this research by demonstrating that economic disadvantage in childhood is also associated with a flatter slope—even after controlling for current demographics and stressors—and that early economic and later economic adversity interacted to predict lower waking cortisol. These findings are novel for diurnal cortisol.

4.1 | Limitations

There are several limitations to the current study. In the current study, childhood maltreatment and economic disadvantage were assessed through retrospective reports. Although this is a common method for reporting on childhood experiences of stress, the validity/utility of using retrospective reports of childhood experiences to predict adult biological and health outcomes is debated. However, retrospective and prospective reports of childhood adversity show moderate agreement with one another (Reuben et al., 2016).

Moreover our study attempts to assess similar experiences of economic and psychosocial stress at past and current time periods. These measures capture overlapping, but not identical aspects of stress. The CTQ assesses current perceptions of past treatment by family members and access to necessities, and is unable to capture the frequency or severity of past stressful life events, whereas the SLES assesses the occurrence of major, but not necessarily traumatizing, stressful life events. Economic disadvantage was also assessed differently between periods, with childhood disadvantage measured through a series of questions about family economic status and adult disadvantage indexed via current self-reported income. Clearly both major and everyday stress matter; however, we did not have a measure of everyday life stress in childhood, nor a measure of major traumatic events in adulthood so we are unable to assess whether one is more important than the other in each time period.

Salivary cortisol was assessed during pregnancy, a period that is associated with increased HPA axis activity. An overall increase in circulating cortisol and adrenocorticotropic hormone (ACTH) makes it challenging to distinguish between maternal and fetal stress biology. However, our findings show a pattern between psychosocial stress and basal cortisol rhythms in mothers, despite the shared environment between the mother and fetus. Lastly, although sampling compliance was measured by an electronic monitoring device, due to technical errors, these data were not available for enough participants to be usable in our study.

Despite these limitations, our study is among the first to examine how developmental and current life stress shape HPA axis functioning through the diurnal cortisol rhythm. Further, our study includes multiple stress domains (i.e., economic and life stress) across different time points, permitting an analysis of whether particular kinds of stressors experienced at specific times are associated with cortisol above and beyond other kinds of stress. In addition, our assessment of current life stress is drawn from an investigator-rated life stress interview, recognized as a best practice for quantifying experiences of stressful events (Vrshek-Schallhorn, Ditcheva, & Corneau, 2019).

Although the current study focuses solely on maternal stress system outcomes, these findings shed light on a possible biological mechanism that would partially explain how maternal psychosocial stress affects their offspring's health and well-being. More specifically, we suggest that both past and present stress is associated with pregnant women's daily cortisol rhythms, which leads to differential fetal exposure of cortisol. As described earlier, intrauterine exposure to maternal psychosocial stress increases risk for preterm birth (Wadhwa, Entringer, Buss, & Lu, 2011), and contributes to dysregulated stress system functioning, behavior problems, and mental health disorders in childhood (Entringer, Buss, & Wadhwa, 2010; Gray et al., 2017; Nazzari et al., 2019). Thus, it is important to consider the generational impact of stress across the lifespan, beyond the implications for maternal health, in future research.

Future research should also investigate more specific timing of developmental experiences and their biological associations, such as in the study by Desantis, Kuzawa, and Adam (2015), which examines the economic stress exposures from several development periods and their relationship with adult cortisol. Prospective studies of maternal stress across the lifespan and diurnal cortisol are also needed (Young et al., 2019). Lastly, stress-sensitive biomarkers other than cortisol, such as those associated with the sympathetic nervous system and immune system, should be examined in relation to stressful life experiences and economic

disadvantage to further elucidate the ways in which psychosocial stress becomes biologically embedded.

5 | CONCLUSION

The current study examined developmental and proximal life stress in a sample of pregnant women in order to better understand the origins of prenatal stress, as indexed by HPA axis dysregulation. Findings revealed that aspects of both developmental and proximal stress were associated with diurnal cortisol, though early life stressors were more robustly associated with diurnal cortisol. We also found evidence that early life and proximal stress interacted to predict waking cortisol, exclusively for economic adversity. Overall, these results have important implications for understanding how economic adversity and other life stressors are embodied within individuals across the lifespan and how stress is transduced across generations.

ACKNOWLEDGEMENTS

This study was funded by the NorthShore University Health System Auxiliary Research Scholar Award, NorthShore Research Career Development Award, Northwestern University Institute for Policy Research and Weinberg College of Arts and Sciences, and Award #HHSN275201200007I—HHSN27500005 of the National Children's Study: Vanguard Study—Task Order 5: Stress and Cortisol Measurement for the National Children's Study (Principal Investigator: Ann E.B. Borders, MD, MSc, MPH). Support to Courtenay L. Kessler was provided by the U.S. Department of Education, Institute of Education Sciences, Multidisciplinary Program in Education Sciences pre-doctoral training grant (R305B140042).

CONFLICT OF INTEREST

The authors declared that they have no conflicts of interest with respect to their authorship or the publication of this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.

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ENDNOTES

[1] Thomas et al. (2018) found that maternal ACEs were also associated with a flattened diurnal slope, but this association did not hold when controlling for proximal stressors.

[2] Participants were excluded from the study if they were taking an oral corticosteroid.

[3] We conducted separate multilevel models for each of the three mood variables: depression (waking: b = 0.001, SE = 0.002, p = .65; diurnal slope: b = 0.001, SE = 0.001, p = .17; 30-min CAR: b= 0.001, SE = 0.003, p = .78); perceived stress (waking: b = −0.001, SE = 0.002, p = .65; diurnal slope: b =0.002, SE = 0.001, p = .11, 30-min CAR: b = 0.001, SE = 0.005, p = .85); and prenatal distress (waking: b = 0.001, SE = 0.003, p = .88; diurnal slope: b =0.001, SE = 0.001, p = .52; 30-min CAR: b =.-0003, SE = 0.003, p = .92).

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How to cite this article: Stephens JE, Kessler CL, Buss C, et al. Early and current life adversity: Past and present influences on maternal diurnal cortisol rhythms during pregnancy. *Dev Psychobiol*. 2020;00:1–15. https://doi.org/10.1002/dev.22000