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## Social Strain and Cortisol Regulation in Midlife in the US

Esther M. Friedman<sup>a</sup>, Arun S. Karlamangla<sup>b</sup>, David M. Almeida<sup>c</sup>, and Teresa E. Seeman<sup>b</sup>

<sup>a</sup>Harvard University

<sup>b</sup>University of California, Los Angeles

<sup>c</sup>Pennsylvania State University

### Abstract

Chronic stress has been implicated in a variety of adverse health outcomes, from compromised immunity to cardiovascular disease to cognitive decline. The hypothalamic pituitary adrenal (HPA) axis has been postulated to play the primary biological role in translating chronic stress into ill health. Stressful stimuli activate the HPA axis and cause an increase in circulating levels of cortisol. Frequent and long-lasting activation of the HPA axis, as occurs in recurrently stressful environments, can in the long run compromise HPA-axis functioning and ultimately affect health. Negative social interactions with family and friends may be a significant source of stress in daily life, constituting the type of recurrently stressful environment that could lead to compromised HPA functioning and altered diurnal cortisol rhythms. We use data from two waves (1995 and 2004-2005) of the Midlife in the U.S. (MIDUS) study and from the National Study of Daily Experiences (NSDE) and piecewise growth curve models to investigate relationships between histories of social strain and patterns of diurnal cortisol rhythms. We find that reported levels of social strain were significantly associated with their diurnal cortisol rhythm. These effects were more pronounced for individuals with a history of greater reported strain across a ten-year period.

### Keywords

U.S.A; Biological markers; Cortisol; Diurnal rhythm; Social relationships; Social strain; Midlife in the U.S. (MIDUS); stress; family

## INTRODUCTION

The role of social support on a variety of health outcomes is well-documented in the sociological, psychological, and epidemiological literatures (see, for example, Anderson and Armstead, 1995; House et al., 1994; Seeman et al., 1985; Uchino et al., 1996). Although attention has focused more heavily on the protective influences of social contact and support, a smaller literature has also documented the negative health consequences of adverse social interactions. Stressful relationships with family and friends, for example, are related to a variety of health outcomes, including functional limitations (Newsom et al., 2008), cardiovascular disease (Coyne et al., 2001; Ewart et al., 1991; Orth-Gomer et al.,

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Please direct all correspondence to Esther M. Friedman, Harvard Center for Population and Development Studies, Harvard University, 9 Bow Street Cambridge, Massachusetts 02138, USA; [friedman@hsph.harvard.edu](mailto:friedman@hsph.harvard.edu).

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2000), decreased immunity (Seeman, 1996), and even mortality (Patterson and Veenstra, 2010; Seeman et al., 1987).

The biological mechanisms through which these health effects of social relationships are thought to operate include influences on the brain and resulting changes in physiological activity in major biological regulatory systems (DeVries et al., 2003; Hofer, 1987; Hofer, 1995; McEwen, 2007). Functional magnetic imaging (fMRI) studies have begun to illuminate the ways in which social relationships are processed by the brain, showing effects on brain processes likely to influence biological systems, including HPA function (Eisenberger et al., 2007; Taylor et al., 2008). One study found that greater reported social support was associated with diminished neuroendocrine reactivity to social stressors (Eisenberger et al. 2007).

Indeed, a growing body of evidence indicates that both positive and negative social relationships influence biology (see Seeman and McEwen, 1996; Uchino, 2006 for reviews). Community-based studies, for example, have linked social support to lower heart rate, systolic blood pressure, serum cholesterol, smaller waist-hip ratios, lower risk of metabolic syndrome, lower urinary cortisol and catecholamines, and sharper, more pronounced diurnal cortisol rhythms (Ryff et al., 2004; Seeman and McEwen, 1996; Sjögren et al., 2006; Vogelzangs et al., 2007). Greater reported social conflict, on the other hand, has been linked to higher blood pressure, cholesterol, inflammation, poorer metabolic profiles, and higher urinary catecholamines and cortisol (Seeman and McEwen, 1996). Experimental evidence similarly shows that positive social relationships decrease cardiovascular and neuroendocrine responses to challenging tasks (Floyd et al., 2007; Grewen et al., 2003) while interpersonal conflict or hostility leads to increased cardiovascular and neuroendocrine reactivity (Gerin et al., 1992; Seeman and McEwen, 1996).

### Why Salivary Cortisol?

Large-scale surveys have increasingly sought to include salivary cortisol assessments to index HPA-axis reactivity. This is because of the centrality of the HPA axis in regulating multiple aspects of human physiology that are critical to health and well-being, and the hypothesized links between such HPA-axis activity and cognitive-emotional responses to the world around us, including importantly our social worlds. Stimuli that activate the HPA function cause an increase in cortisol which triggers downstream physiological responses that help provide the energy and physiological resources needed to adapt to that stimulus. Activation of cortisol also helps to contain other components of the physiological stress response such as increases in inflammatory processes which, if unchecked, can themselves have negative health consequences. Thus, short-term activation of the HPA axis is necessary for optimal everyday physiological functioning. However, recurrent or chronic activation of this system has been linked to increased risks for a variety of adverse health outcomes, including cardiovascular disease, diabetes, cancer, cognitive decline, and reduced immune function (for a review, see McEwen and Seeman, 1999). In addition, the diurnal rhythm is sensitive to and altered by a variety of stressful situations (Adam and Gunnar, 2001; Steptoe et al., 2003; Vedhara et al., 2000).

Earlier work on the relationships between cortisol and health has focused on average cortisol measures with an interest in cortisol levels over the entire day. This is the approach used, for example, when collecting urinary cortisol, which involves one cortisol sample that is an aggregate measure of, typically, 12 - 24 hours of cortisol (Seeman et al., 2002). With the advent of salivary cortisol protocols, research has examined patterns of cortisol activity at multiple times of the day for one or more days. Such data capture what is typically referred to as the “cortisol diurnal rhythm.” The diurnal rhythm is characterized by a rapid increase in cortisol over the first 30-45 minutes after waking, followed by a rapid decline over

approximately the next two hours and then a slower decline through the late afternoon and evening. Younger, healthier individuals show a more pronounced diurnal rhythm with a higher morning peak and a lower night-time nadir and less healthy and older individuals have a flatter curve (Adam and Kumari, 2009). Examining salivary cortisol over the course of the day provides a more complete picture of cortisol regulation (or dysregulation). In fact, one of the primary advantages of salivary cortisol samples over urinary or blood samples is that they allow for repeated and unobtrusive measurement of cortisol over multiple times of the day (Almeida, McGonagle et al. 2009).

### **Prior Research on Social Relationships and Cortisol**

The influence of social relationships on cortisol response has been a topic of interest in both human and animal research. Animal research has long suggested that contact with others of the same species plays a critical role in successful development, and animals demonstrate the potential for both positive and negative health effects of the social environment (Cassel, 1976; Henry et al., 1967; Levine, 1993). To date, research examining social support and cortisol in human populations has largely taken experimental approaches. Experimental manipulations provide strong evidence that social contact or support from a friend or partner during challenge tests (such as math or public speaking tasks) *decreases* neuroendocrine responses, including cortisol (Seeman and McEwen, 1996, Grewen et al., 2003; Uchino et al., 1996). In contrast, reported inadequate support has been linked to *greater* physiological reactivity, again including cortisol responses to laboratory-based challenge tests (Nausheen et al., 2007; Seeman and McEwen, 1996; Uchino et al., 1996).

Community-based and, more recently, population-level studies have also begun to focus on associations between aspects of the social environment and cortisol regulation. For instance, one community-based study of social strain and urinary cortisol found that increased frequency of demands and criticism was positively related to overnight urinary cortisol levels for men but not women (Seeman et al., 1994). Greater reports of hostility and cynicism are related to higher levels of cortisol in the daytime (Pope and Smith, 1991; Ranjit et al., 2009). In addition, social relationships with parents in childhood may have lasting effects on cortisol levels well into middle and later life (Repetti et al., 2002; Taylor et al., 2011).

One of the difficulties in investigating the relationship between social stressors and salivary cortisol is that salivary cortisol must be measured at multiple time points over the day, and there are therefore many different measures of cortisol that may be used to capture a dysregulated rhythm. One might think about dysfunction in the morning awaking response as a blunted peak, a slower decline in cortisol levels in the evening, or as a measure of accumulated daily cortisol, such as the area under the curve. For the most part, the influence of social factors on cortisol appears to be strongest for measures capturing cortisol decline over the course of the day, particularly for the evening and resting cortisol levels (Adam and Kumari, 2009; Seltzer et al., 2009). Blunting of the diurnal rhythm over the day (lower peak and higher nadir) occurs systematically with age, and this same blunted rhythm is also evident for individuals exposed to frequent life stresses (Birditt et al., 2011; Varadhan et al., 2008). We therefore hypothesize that individuals with greater levels of social strain will show a flatter cortisol rhythm overall, and show particularly pronounced dysregulation in the latter part of the day.

### **Conceptualization of Social Strain**

Social strain may be conceived of in a variety of ways. It can be thought of as network stress, problematic social exchanges, or interactions with network members that induce psychological distress. In keeping with Goffman's analysis of "face work," we treat social

strain as a characteristic of interactions that “is neither inherent nor a permanent aspect of the person” (Trevino, 2003, p. 37). The index of social strain that we use makes no assumption regarding the respondent’s inherent qualities; it simply reflects the person’s varied self-reported perceived experiences of critical, irritating, or other negative interactions with significant others in his or her social milieu. These experiences, we hypothesize, have adverse consequences that linger in the individual’s biological repertoire.

## DATA AND METHODS

The National Survey of Midlife Development in the United States (MIDUS) study was initiated in 1995 to determine how social, psychological, and behavioral factors interrelate to influence mental and physical health. The first wave (1995) collected socio-demographic and psychosocial data on 7,108 Americans, ages 25 to 74 years, from a representative sample of English-speaking, non-institutionalized adults residing in the contiguous 48 states, with oversampling of five metropolitan areas, twin pairs, and siblings.

Of the original 7,108 MIDUS participants, 4,963 were successfully re-contacted in 2004-2005 and completed the MIDUS II 30-minute phone interview and two self-assessment questionnaires 9-10 years later using the original protocol (Love et al., 2010). In this wave, a random sub-sample (n=1,605) also completed short telephone interviews about their daily experiences over eight consecutive days and collected saliva (for cortisol assessments) on four of the eight days. This National Study of Daily Experiences (NSDE) subsample and the MIDUS sample from which it was drawn had very similar distributions for key demographic factors (see Almeida et al., 2002).

### Salivary Cortisol

Respondents received a Home Saliva Collection Kit one week prior to their initial phone call. In addition to written instructions, telephone interviewers reviewed the procedures and answered any of the participant’s questions. On days two through five, respondents provided four saliva samples per day that were later assayed for cortisol. Respondents took these samples in their own home, by placing a roll of cotton in their mouths, chewing on it for approximately 30 seconds, and placing it in a tube called a salivette, which respondents stored at room temperature until they were returned to the clinic the next day. Saliva was collected immediately upon waking, 30 minutes after waking, before lunch, and before bed. Data on the exact time respondents provided each saliva sample was obtained from the nightly telephone interviews as well as on a paper-pencil log sent with the collection kit. In addition approximately a quarter of the respondents received a “Smart Box” containing a computer chip that recorded the time respondents opened and closed the box (See Almeida, MacGonagle et al., 2009 and Almeida, Piazza et al., 2009). In our analyses, we use information on collection time from the home collection sheet times, unless they are missing, in which case the times reported in the interview are used instead. For all analyses, cortisol is recoded as the  $\ln(\text{cortisol}+1)$ , in order to account for outlying cases and some small cortisol values.

We began with an initial NSDE sample of 1,605 participants with 6,383 days of cortisol data. We dropped days that appear to reflect time-recording error for one of the saliva samples or saliva sample, days when respondents woke unusually early, late, or remain awake for more than 20 hours, values outside of the normal range (i.e. >60 nmol/L), which likely reflect either errors or the effects of medications, and individuals with missing predictor/covariate data. This left us with a final sample of 1,502 people, 5,629 days and 21,741 total saliva measurements. Respondents in the final sample had at least one valid salivary sample of cortisol, with some respondents providing as many as sixteen samples (four on each of four days).

## Longitudinal Reports of Social Strain

Adult social strain with family and friends were assessed from items in the self-administered mail questionnaires in the MIDUS data in 1995 (before collection of cortisol) and 2005 (concurrent with cortisol collection). Participants' perceptions as to the frequency of various types of social strain were queried with respect to relationships with spouse/partner (6 items), friends (4 items), and other family members (4 items). The items include the following: "How often do your *friends/spouse/family* make too many demands on you?"; "How often do they criticize you?"; "How often do they let you down when you are counting on them?"; "How often do they get on your nerves?" For the spouse/partner scale, two additional items are included: "How often does he or she argue with you?"; and "How often does he or she make you feel tense?".

All items are measured on a four point scale indicating whether this occurs 1 Often; 2 Sometimes; 3 Rarely; or 4 Never. The mean of all items was calculated for each relationship type (i.e. spouse, family, friends), with items recoded so that higher scores reflect higher strain. We then averaged the three scales into one global score measuring the respondent's average level of social strain from all sources ( $\alpha = 0.86$ ).

In addition to constructing separate strain scores for each wave, we also combined the scores for the two waves by dividing each wave's scores into quartiles and constructing a score across the two waves using the following coding:

1. Not in the highest quartile of strain in either Wave 1 or 2
2. Highest quartile strain in Wave 1 only
3. Highest quartile strain in Wave 2 only
4. Highest quartile strain in both waves

This construction allows us to distinguish subgroups on the basis of their joint patterns of reported frequency of social strain at both MIDUS I and MIDUS II. Though these designations do not account for variations in the frequency of social strain between the two waves, the information from these two time points nonetheless provides important longitudinal information, allowing us to distinguish those reporting more cumulative social strain (at least as indicated by reported high levels of social strain at both waves) – a group we hypothesized would be at highest risk for the biological consequences of social strain.

## Control Variables

Multivariable analyses also include controls for race, age, sex, and education. Both race and sex were coded as dichotomous indicator variables, with the first indicating whether a respondent was white or nonwhite and the latter, whether male or female. A three category age variable was included in the models with age coded as <50 years old, 50-64, and 65+. Education was included in all models as three dummy variable indicating whether the respondent completed (1) high school or less schooling; (2) some college; or (3) college degree or more (16+ years of education).

## ANALYSES

Because previous studies indicate that cortisol rhythms are driven by time elapsed since awakening and less by clock time (van Cauter, 1990; Kumari et al., 2010), we examined cortisol trajectories as a function of time since waking. Based on visual examinations of average cortisol rhythms in the sample and in demographic strata defined by age, gender, race, and socioeconomic status and in line with other work (Hajat et al., 2010; Taylor et al., 2010), we modeled the diurnal cortisol trajectories as piecewise linear growth curves, using

four linear splines with three knots, fixed at 0.5 hours, 4.5 hours, and 15 hours after waking. The four spline pieces represent four phases of the day, with the first piece representing the morning rise (waking to half hour after waking); the second, a steep early decline (0.5 to 4.5 hours after waking); the third, a more gradual late afternoon through evening decline (4.5 to 15 hours after waking); and the final piece representing a later night plateau (15 to 20 hours after waking).

The intercept (representing the waking value) and all four spline slopes were modeled as functions of the primary predictor (social strain) and covariates. In order to remove any bias that may arise from differences in sleep patterns, all models include controls for sleeping and waking habits based on information obtained from the log maintained by the participant. These variables include the length of sleep the previous night, whether the respondent woke before the median wake up time of the sample, night bedtime, and whether or not it was a weekend day (for those who were employed). To capture the influence of too little and too much sleep, we categorized the previous night's sleep into three groups: <6 hours, 6-8 hours, and >8 hours. Waking time and bedtime were used to compute the length of the waking day, which was averaged over all eight dairy days, to get average wake-day length for every participant. We control for these sleep-related variables in particular, because preliminary analyses indicated that the shape of the diurnal trajectories differed for these groups.

We used hierarchical, 4-level, linear mixed effects models to fit the cortisol growth curves and to account for within-individual, within-family (MIDUS included some siblings and twins), and within-day clustering. To account for the correlation between repeated measures of cortisol in the same individual (between 1 and 16 measurements per person), we included random effects for the intercept (wakening value of cortisol) and all four slopes. We also include a level for correlations between samples on the same day, along with random effects for the intercept and the second slope. Finally, to allow for correlation between members of the same family, we included an additional hierarchical level with random intercept. Model-predicted intercept and slopes were used to estimate mean values for other trajectory parameters, such as the magnitude of the daily peak, the nightly nadir, and the total cortisol exposure over 16 hours since waking, which we refer to as the area under the curve (AUC). We do not include the late night plateau in our calculations of the area under the curve as this is only available for select respondents who stay up more than 15 hours. The AUC was calculated using the trapezoidal rule (Yeh and Kwan, 1978), where the total AUC is the sum of the areas of several individual trapezoids. Estimates were calculated as follows:

$$\begin{aligned} \text{Peak} &= \text{Intercept} + 0.5 * \text{slope}_1 \\ \text{Nadir} &= \text{Peak} + 4 * \text{slope}_2 + 10.5 * \text{slope}_3 \\ \text{AUC} &= 0.25 * (\text{Intercept} + \text{Peak}) + 2 * (2 * \text{Peak} + 4 * \text{slope}_2) + 5.25 * (\text{Peak} + 4 * \text{slope}_2 + \text{Nadir}) + 0.5 * (2 * \text{Nadir} + 1 * \text{slope}_4) \end{aligned}$$

Slope<sub>1</sub>, Slope<sub>2</sub>, Slope<sub>3</sub>, and Slope<sub>4</sub> refer to the model-estimated mean slopes (per hour) for the four piece-wise linear segments of the trajectory.

## RESULTS

Table 1 provides descriptive information on the model variables for the analytic sample. Approximately 30 percent of participants were less than 50 years old at the time of the MIDUS II data collection, 40 percent were between 50 and 65 and nearly 30 percent were 65 and older. The sample was largely White and relatively well-educated, with over 40 percent having a college degree. There was substantial variance in reported social strain. For Wave 1, the average level of social strain across all relationship types was 2.05 (equivalent to responses of “rarely”). In Wave 2 the corresponding value was 1.98. The lowest levels of

mean strain were for friends and the highest for spouse. The 10-year history of social strain in quartiles shows that although most people do not experience extreme levels of social strain, just over 13 percent of respondents are in the highest quartile of strain in both waves.

Figure 1 shows the model-predicted diurnal cortisol rhythm as a function of time since waking in hours for the null model, with inflexions at 0.5 hours, 4.5 hours, and 15 hours. These results are from a model controlling for early waking (waking before median), sleeping fewer than 6 hours the night before, sleeping more than 8 hours the night before, average hours awake, and weekend vs. weekday (if employed), but does not include demographic controls.

This figure shows the expected morning rise, or the cortisol awakening response, from waking until about half an hour after waking, followed by a rapid decline until 4.5 hours after waking, followed by a more gradual late afternoon decline until 15 hours after waking and finally, for respondents who are awake more than 15 hours we find a flattening of their cortisol rhythm to a late night plateau. The first three slopes are statistically significantly different from zero at  $p < 0.01$ ; slope 4 was not statistically different from zero. Model-predicted mean wakening value, peak and nadir, are 13.88 nmol/L, 19.09 nmol/L, and 2.00 nmol/L respectively. Estimated area under the log-cortisol curve (AUC) was 29.39  $\ln(\text{nmol/L} + 1)$ -hours.

Table 2 shows the results of our fully-adjusted models predicting Wave 2 salivary cortisol over the day as a function of Wave 2 social strain scores. This table displays the association between concurrent social strain on the waking value (intercept) and the four slopes, as well as the model estimated peak (highest point), nadir (lowest point) and the full area under the curve for the day (AUC). We present results for mean strain (averaged across spouse, family, friends). Measures are treated as continuous in these models (range: 1 to 4). These results provide a cross-sectional snapshot of the relationship between the cortisol rhythm and social strain.

As Table 2 reveals, respondents reporting higher levels of social strain have a less rapid late day decline (less negative slope) and a higher nadir, suggesting that their cortisol levels do not come down as much in the evening hours as they do for their counterparts reporting lower levels of social strain. Higher levels of social strain are also associated with a somewhat (marginally significant) lower morning peak value. Taken in combination, these results suggest that respondents with higher levels of social strain exhibit a blunted cortisol rhythm over the day. That is, cortisol values do not go up as much in the early morning hours, do not come down as much later in the evening before bedtime, and do not reach as low a nadir as they do for individuals with lower levels of social strain. For instance, an individual with a mean strain score of four, who *often* experiences strain with family and friends, has a peak log cortisol value that is 0.31 standard deviations ( $2 * 0.052 / 0.337$ ) lower than that of a matched counterpart with a mean strain score of two (who rarely experiences strain with family and friends). This difference in peak log cortisol translates to 10 percent reduction in peak cortisol ( $e^{-0.052 * 2} = 0.90$ ). The log cortisol nadir, on the other hand, is 0.33 standard deviations higher and the nadir is 15 percent higher for those with frequent strain (mean strain score of 4) compared to those with average levels of strain (mean of 2). To put this in perspective, differences in peak log-cortisol between those reporting high versus low social strain (for a two unit difference in strain, effect size = 0.31 standard deviations) is comparable to the differences between those with high school or less versus college or more education (effect size = 0.27 standard deviations), while the differences in log-cortisol nadirs between those with high vs. low social strain is 3 times larger than that seen for high school or less versus college or more-educated individuals (effect size 0.33 vs. 0.14 standard deviations).

These analyses indicate that the associations between social strain and cortisol are strongest for cortisol measures capturing the decline in cortisol over the latter part of the day. Over the day as a whole, cortisol rhythms are generally flatter for those with higher reported strain than for their counterparts with lower level of reported strain with family and friends. This pattern can also be seen in Figure 2.

Figure 2 shows the predicted cortisol trajectories over the course of the day for a predicted mean strain score of 1 (“never”), 2 (“rarely”), and 3 (“sometimes”). The average of the mean strain score for the analytic sample was 2 (see Table 1). Although all three groups show clear diurnal rhythms with a morning rise and a later day decline, the most pronounced trajectory is apparent for the lowest strain group, the flattest trajectory is for highest strain group, and those with mean levels of reported strain fall directly in between the other two groups.

In results not shown here, we also ran the model described above, with the addition of a difference score measuring the change in strain between Waves 1 and Wave 2. The coefficients for the change score were not statistically significant. In addition, the significant values for the Wave 2 cortisol slopes remained strong and were sometimes even strengthened when the difference score was added. This suggests that it is Wave 2 levels of social strain that are most strongly related to Wave 2 cortisol, and that the change between the two waves does not explain the relationship between Wave 2 social strain and cortisol rhythm, though the relatively high stability in reports of strain makes it difficult to evaluate the impact of changes in strain.

### Patterns of Social Strain over Two Waves

Another way to bring in information from both waves of social strain is by classifying respondents into categories based on whether they were in the highest quartile of social strain in Wave 1 only, Wave 2 only, both waves, or in neither wave. Looking at individuals in the highest quartile of strain allows us to assess how much experiencing extreme levels of social strain (as reported at two time points a decade apart) is related to cortisol dysregulation over the course of the day. By bringing together the two waves of information, the MIDUS data allow for a richer, longitudinal assessment of differences in reported frequencies of social strain based on data obtained approximately a decade apart. This allowed us to differentiate those who reported the highest frequencies of social strain at both interviews from those with either “mixed profiles” (i.e., reporting higher frequency at one or the other but not both waves) or consistent profiles of low reported frequency of social strain, and to examine how the association between social strain and cortisol might vary as a function of these longitudinal profiles of reported social strain.

Table 3 shows the results of spline models predicting the cortisol diurnal rhythm as a function of 10-year history of social strain, assessing whether respondents were in the highest quartile of strain in Wave 1, Wave 2, both waves, or neither wave (reference category). This table shows the coefficients and standard errors for the waking values, the four slopes during the day, and the model estimated peak, nadir, and AUC.

Compared to those reporting lower levels of social strain at both waves, those reporting the highest levels of strain at both waves exhibit significantly slower late day declines and marginally higher waking, peak and nadir values. They also have higher waking and nadir values than do those with higher strain only at Wave 2. Somewhat unexpectedly, we also saw a stronger association of “Wave 1 only” high levels of conflict on cortisol regulation than for “Wave 2 only” high conflict. Compared to those who were never in the highest quartile of reported strain, individuals with social strain only in Wave 1 exhibited slower rates of late afternoon decline (slope 3) but more negative later night slopes; they also had

marginally higher nighttime nadir values. Those who have high strain in Wave 2 only, on the other hand, do not differ significantly from individuals who are never in the highest quartile of strain.

## DISCUSSION

This paper examines hypothesized relationships between frequency of strain in salient social relationships and patterns of diurnal cortisol regulation. Findings suggest that individuals who perceive more frequent social strain in relationships with spouse, family and close friends are at increased risk for poorer cortisol regulation. Their cortisol levels do not go up as much in the early morning hours, do not come down as much later in the evening before bedtime, and do not reach as low a point as they do for individuals with lower levels of strain. All in all, their rhythms are flatter than those of their counterparts.

We looked at strain at a point in time and as a ten-year cumulative history to get a complete picture of the role of strain in cortisol dysregulation. Lab-based data already support cortisol's immediate responsiveness to short term strain (Gruenewald et al., 2004; Kirschblum et al., 1992). Our study shows that there are long term implications of persistent exposure to social stressors. Cross-sectionally, someone with a mean strain score of four, who reports often experiencing strain with family and friends, exhibits a peak cortisol value that is nearly 10 percent lower and a nadir that is 15 percent higher than a counterpart with a mean strain score of two (equivalent to rarely). These effects, particularly for the latter part of the day, are more pronounced for those individuals who consistently report high levels of strain over time. Our findings also suggest that there may be a lag in the impact of social strain on dysregulations in neuroendocrine functioning – more persistent strain and earlier strain showing associations with later cortisol dysregulation whereas Wave 2 only strain (concurrent with cortisol measurements) has yet to show such effects.

These findings add to the growing literature showing that social influences are critical for healthy physiological functioning (Robles et al., 2006, Seeman and McEwen, 1996). For instance, Robles and colleagues (2006) examine conflict between spouses in a laboratory setting and find that supportiveness during negative interactions between couples promotes adaptive physiological responses to interpersonal conflict. Seeman and McEwen (1996) show that social contact and support during high stress tasks (such as math or public speaking) decreases neuroendocrine responses, while inadequate support increases physiological reactivity. Our work looks at a larger, more representative sample of the population, and investigates cortisol regulation in daily life. We find that strained interpersonal relationships with family and friends have significant consequences for HPA regulation.

Consistent with the aspects of cortisol rhythm that we found to be most dysregulated for individuals who report greater social strain, flattened cortisol rhythms especially in the latter part of the day have been linked to a variety of physical health outcomes (Brunner et al., 2002; Matthews et al., 2006; Smith et al., 2005), depression (Herbert et al., 2006; McEwen, 2007), cognitive decline (Seeman et al., 1997), and even mortality (Kumari et al., 2011). Our findings are therefore consistent with the notion that strained social relationships have implications for health. This is in line with the broader idea that such effects on cortisol may reflect one of the pathways through which social relationships affect major morbidity and mortality.

Several limitations of this paper should be acknowledged. First, although we have information on social strain over two waves of data, we only have cortisol measures at one point in time. Without longitudinal data on cortisol, it is impossible to determine whether

there is a causal relationship between social relationships and cortisol diurnal rhythm. Second, although we have two waves of data in which we can investigate social strain, we do not have a true history of strain over that time period, but only have two time points separated by ten years. Ideally, we would like to have more frequent measures of strain over that time period to get a richer picture of differences in chronic social strain. However, this lack of information should, if anything, result in greater measurement error as we have information for only two time points, and thus weaken our ability to detect a relationship to cortisol.

Despite these caveats, this work has important implications for the growing body of work showing a link between social relationships and health. This paper looks beyond social relationships at a point in time and shows that cumulative social strain over the long run is associated with poorer diurnal cortisol regulation- a potentially important contributor to downstream health. Our findings suggests that a longer-term perspective on social relationships and health is necessary for understanding the lasting effects of negative social relationships and to get a more complete picture of how health inequalities develop within societies. This paper only considers social relationships at two points over a ten-year period. Future work should examine how social relationships over the life course – from childhood on – translate into accumulated impacts on health and well-being in midlife and beyond.

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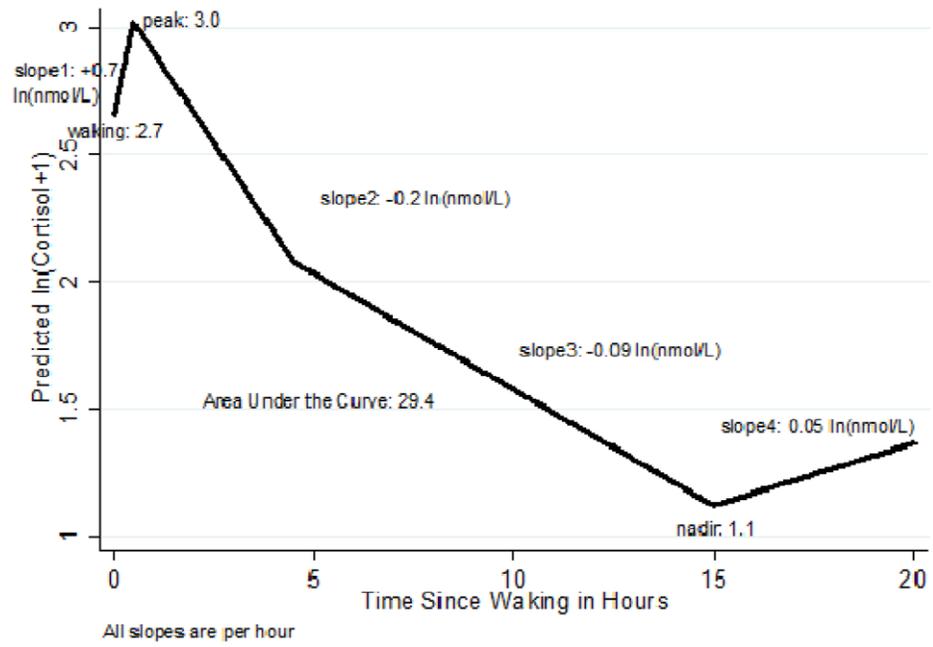
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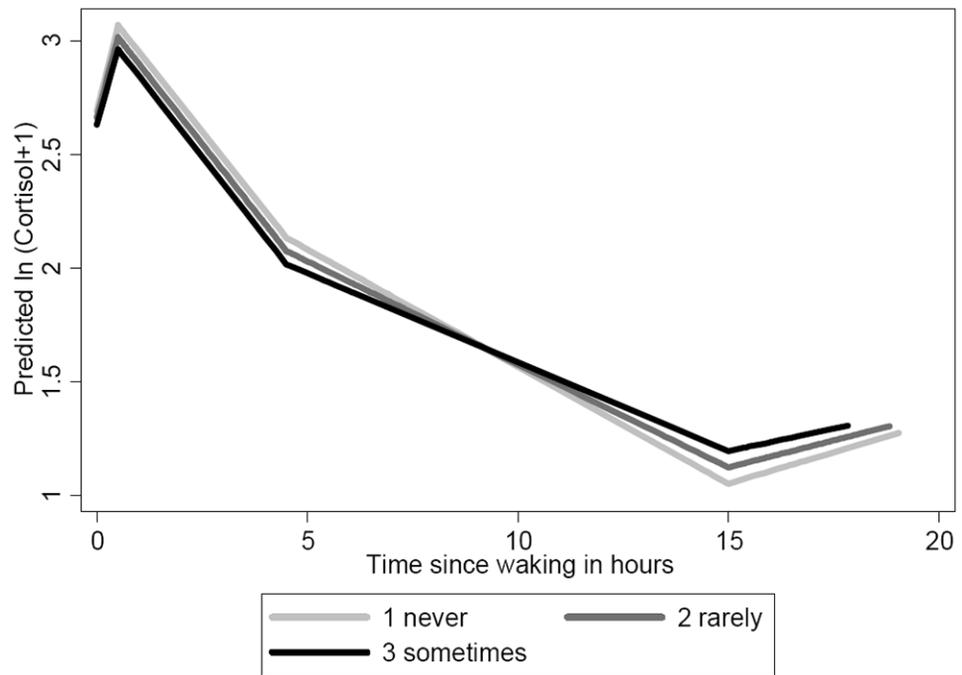
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### Research Highlights

- Negative social interactions may be a significant source of stress and could lead to altered diurnal cortisol rhythms.
- This study investigates the association between two waves (ten-years) of perceptions of social strain and cortisol rhythms in midlife.
- We find that reported levels of social strain were significantly associated with diurnal cortisol rhythm.
- These effects were more pronounced for individuals with a history of social strain across a ten year period.



**Figure 1.**  
Predicted Cortisol Diurnal Rhythm for the Null Model (n=1,502)



**Figure 2.**  
Predicted  $\ln(\text{Cortisol}+1)$  (nmol/L) Over the Day by Wave 2 Mean Social Strain Score  
( $n=1,502$ )

**Table 1**

Descriptive Statistics for Analytic Sample (n=1,502)

Variable		Unit or Category	Percent
Demographics	Age	<50	30.83
		50-65	40.68
		65+	28.50
	Sex	Male	44.07
		Female	55.93
	Race	White	93.01
		Non-white or mixed race	6.99
	Education	High school degree or less	29.29
		Some college	29.36
College degree+		41.35	
			<u>Mean (sd)</u>
Wave 1 Social Strain	Spouse only (n=1,178)	Range, 1-4	2.22 (0.60)
	Friends only (n=1,501)	Range, 1-3.75	1.90 (0.48)
	Family only (n=1,498)	Range, 1-4	2.08 (0.58)
	Mean Strain (n=1,502)	Range, 1-3.58	2.05 (0.43)
Wave 2 Social Strain	Spouse only (n=1,151)	Range, 1-4	2.15 (0.61)
	Friends only (n=1,493)	Range, 1-3.50	1.81 (0.49)
	Family only (n=1,497)	Range, 1-4	2.01 (0.58)
	Mean Strain (n=1,502)	Range, 1-3.64	1.98 (0.44)
			<u>Percent</u>
10-Year History of Social Strain	Spouse Only (n=1,117)	Never highest quartile strain	66.61
		Highest quartile strain wave 1 only	9.67
		Highest quartile strain wave 2 only	14.06
		Highest quartile strain both waves	9.67
	Friends Only (n=1,492)	Never highest quartile strain	71.92
		Highest quartile strain wave 1 only	6.23
		Highest quartile strain wave 2 only	14.61
		Highest quartile strain both waves	7.24
	Family Only (n=1,495)	Never highest quartile strain	69.70
		Highest quartile strain wave 1 only	6.89
		Highest quartile strain wave 2 only	14.04
		Highest quartile strain both waves	9.36
	Mean Strain (n=1,502)	Never highest quartile strain	64.65
		Highest quartile strain wave 1 only	11.12
		Highest quartile strain wave 2 only	10.79
		Highest quartile strain both waves	13.45

**Table 2**  
Coefficients and Standard Errors from Spline Models of log cortisol+1 (nmol/L) as a Function of Wave 2 Social Strain, (n=1,502)

	Waking Value	Slope 1: Morning Rise	Slope 2: First Decline	Slope 3: Late Day Decline	Slope 4: Late Night Plateau	Peak	Nadir	AUC
Mean:	2.661	0.711	-0.236	-0.092	0.048	3.016	1.104	29.390
SD:	0.320	0.183	0.0461	0.030	0.048	0.337	0.433	5.414
Mean Strain	-0.032 (0.025)	-0.041 (0.043)	-0.002 (0.007)	0.012** (0.004)	-0.008 (0.020)	-0.052 <sup>+</sup> (0.027)	0.072 <sup>+</sup> (0.043)	-0.109 (0.469)
Male	0.109** (0.022)	-0.169** (0.037)	0.031** (0.006)	-0.006 <sup>+</sup> (0.003)	-0.034 <sup>+</sup> (0.017)	0.025 (0.024)	0.089* (0.038)	1.707** (0.413)
Age (ref: <50)	0.007 (0.027)	0.127** (0.043)	-0.003 (0.007)	0.003 (0.004)	-0.032 (0.020)	0.071* (0.028)	0.090* (0.045)	1.149* (0.494)
65 <sup>+</sup>	0.069* (0.030)	0.165** (0.050)	0.017* (0.008)	0.010* (0.004)	-0.034 (0.024)	0.151** (0.0319)	0.328** (0.050)	3.978** (0.552)
White (ref: Non-white)	0.146** (0.042)	-0.153* (0.072)	-0.029* (0.012)	-0.007 (0.007)	-0.032 (0.031)	0.069 (0.046)	-0.124 <sup>+</sup> (0.073)	-0.940 (0.791)
Education (ref: College+)	-0.142** (0.027)	0.103* (0.045)	0.012 <sup>+</sup> (0.007)	0.010* (0.004)	-0.023 (0.021)	-0.090** (0.029)	0.060 (0.046)	-0.187 (0.499)
Some college	-0.073** (0.026)	0.009 (0.044)	0.018* (0.007)	-0.001 (0.004)	0.022 (0.021)	-0.068* (0.028)	-0.007 (0.045)	-0.184 (0.491)

Notes: To assist with interpretation of effect sizes, the sample means and standard deviations for the parameters of the diurnal trajectory of log(cortisol) are listed under the column headings. These means and standard deviations came from a null model without demographic controls. Units for level values (waking, peak, nadir) are log (nmol/L). Units for slopes are log (nmol/L) per hour. Unit for AUC is log(nmol/L)-hour.

Standard errors in parentheses.

Models also control for wake before median wake time, number of hours awake (centered), whether weekend, slept fewer than six hours or more than eight hours the night before.

<sup>+</sup> p<.10,

\* p<.05,

\*\* p<.01

Table 3

Coefficients and Standard Errors from Spline Models of log cortisol+1 (nmol/L) as a Function of 10-yr History of Social Strain (n=1,502)

	Waking Value	Slope 1: Morning Rise	Slope 2: First Decline	Slope 3: Late Day Decline	Slope 4: Late Night Plateau	Peak	Nadir
Mean:	2.661	0.711	-0.236	-0.092	0.048	3.016	1.104
SD:	0.320	0.183	0.0461	0.030	0.048	0.337	0.433
Mean Strain (reference: never highest quartile)							
Highest Quartile Wave 1 Only	-0.026 (0.035)	-0.001 (0.010)	0.010* (0.005)	-0.061* (0.027)	0.008 (0.034)	0.112 <sup>+</sup> (0.059)	0.700 (0.636)
Highest Quartile Wave 2 Only	0.056 (0.035)	-0.008 (0.010)	0.005 (0.005)	0.018 <sup>†</sup> (0.027)	0.028 (0.037)	0.047 (0.060)	0.341 (0.647)
Highest Quartile Both Waves	-0.058 <sup>+2</sup> (0.033)	-0.013 (0.056)	0.013* (0.005)	0.008 <sup>†</sup> (0.026)	-0.057 <sup>+2</sup> (0.035)	0.096 <sup>+</sup> (0.055)	0.174 (0.601)

Notes: To assist with interpretation of effect sizes, the sample means and standard deviations for the parameters of the diurnal trajectory of log(cortisol) are listed under the column headings. These means and standard deviations came from a null model without demographic controls. Units for level values (waking, peak, nadir) are log (nmol/L). Units for slopes are log (nmol/L) per hour. Unit for AUC is log(nmol/L)-hour.

Standard errors in parentheses. Models also control for wake before median wake time, number of hours awake (centered), whether weekend, slept fewer than six hours or more than eight hours the night before, sex, age categories, white vs. nonwhite, education categories.

<sup>+</sup> p<.10,

\* p<.05,

\*\* p<.01

<sup>†</sup> Differs significantly from 'highest quartile wave 1 only' group at p<0.05

<sup>2</sup> Differs significantly from 'highest quartile wave 2 only' group at p<0.05