How Does Bereavement Get Under the Skin? The Effects of Late-Life Spousal Loss on Cortisol Levels

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Objectives. We used data from the Changing Lives of Older Couples, a prospective multiwave study of 1,532 married individuals aged 65 and older, to investigate the extent to which spousal loss and death-context characteristics are associated with the stress hormone cortisol at 6 (W1) and 18 (W2) months postbereavement.

Method. We used ordinary least squares regression models to estimate the effects of death-context characteristics (forewarning, caregiving, and postloss numbness, reported at W1) on cortisol levels (at W1 and W2). We included age and gender and evaluated a two-way interaction term between gender and death circumstances.

Results. Bereaved spouses who reported prolonged forewarning of the death evidenced higher cortisol levels at W1 than those who did not experience prolonged forewarning. Bereaved women had higher cortisol levels than bereaved men at W1. A two-way interaction between gender and emotional numbness was statistically significant, where men (but not women) who experienced postloss numbness had elevated cortisol levels at W2.

Discussion. Our findings reveal that stressful life events are associated with stress-related neuroendocrine reactions for longer durations than researchers have previously documented. The specific death-related stressor affecting cortisol varies by gender. Implications for research and practice are discussed.

Key Words: Bereavement—Caregiving—Cortisol—Stress—Widowhood.

THE deleterious effects of late-life spousal loss on mental and physical health are well-documented (Buckley, McKinley, Tofler, & Bartrop, 2010). Studies using cross-sectional designs report associations between widowhood and biological functioning (Irwin, Daniels, Risch, Bloom, & Weiner, 1988). Longitudinal analyses also document elevated risk of mortality, morbidity, and cardiovascular problems after bereavement, even after age is controlled (Buckley et al., 2010; Williams, 2004). Recent studies identify specific aspects of the dying process that are particularly harmful to the bereaved, including intensive preloss caregiving and a prolonged dying process (Bennett, 2006; Carr, House, Wortman, Nesse, & Kessler, 2001). However, little is known about the underlying physiological mechanisms that account for these health effects or their time course. One plausible mechanism is dysregulation of the hypothalamus adrenal axis (HPA) and secretion of cortisol (Michaud, Matheson, Kelly, & Anisman, 2008). We propose that chronic stressors that precede spousal loss, such as spousal caregiving, and emotional reactions that follow the loss, activate the HPA system and are associated with elevated cortisol levels (Ong, Fuller-Rowell, Bonanno, & Almeida, 2011; Piazza, Almeida, Dmitrieva, & Klein, 2010).

Mounting research documents the critical role that cortisol levels may play in linking social stressors to physical health. Cortisol responses are powerful predictors of physical health; for example, high basal levels of urinary cortisol are associated with greater mortality from heart disease in older persons (Vogelzangs et al., 2010), whereas low levels are associated with fatigue (Cleare, Blair, Chambers, & Wessely, 2001). Studies also have found associations between elevated cortisol levels and compromised immune systems, premature aging, and earlier onset of age-related conditions, including cardiovascular disease, osteoporosis, type II diabetes, and functional decline (Glaser & Kiecolt-Glaser, 2005).

Cortisol, a stress hormone, is positively associated with age (Otte, Hart, Neylan, Marmar, Yaffe, & Mohr, 2005; Van Cauter, Leproult, & Kupfer, 1996), being female (Kudielka & Kirschbaum, 2005; Otte et al, 2005) and with both physiological (hypertension, regulation of the immune system) and psychological (affective) disturbances (McEwen, 2003). Previous studies have found that cortisol levels increase with age and that corticosteroid-binding globulin (a protein that facilitates transport of cortisol in the body) levels tend to be higher among older women than among

older men although no gender differences have been found among younger adults (Epel, Burke, & Wolkowitz, 2007; Kudielka & Kirschbaum, 2005). The associations among gender, age, and stress response in later life are complex. In a review of studies exploring sex differences in HPA responses to stress, Kudielka and Kirschbaum (2005) concluded that men have greater stress reactivity to cortisol than women. Taken together, these findings would suggest that the overall gender gap detected in cortisol levels among older adults might be offset by men's stronger reactions to psychosocial stressors, which presumably increase their cortisol levels.

Another complexity detected in studies of stress, aging, and cortisol is that the association between a stressor such as bereavement and cortisol may change as time elapses after the event. Further, the effects of the stressor may vary based on the larger social context, including whether the stressor preceded a long period of chronic stress, such as caregiving during spousal illness. Such fine-grained distinctions in the physiological responses of bereaved spouses may be concealed in studies that do coarse contrasts of widowed and married persons; they may fail to capture important sources of heterogeneity. Addressing these unresolved questions is important for bereavement and stress researchers who study neuroendocrinological responses.

Prior studies of physiological responses to bereavement vary based on the sample and measures used (Roy, Gallucci, Avgerinos, Linnoila, & Gold, 1988; Spratt & Denney, 1991). For example, bereaved family members have been found to evidence higher levels of cortisol, relative to those in a control group (Gerra et al., 2003). However, variation is detected even among the bereaved. Those with high harm-avoidant temperament scores had higher cortisol responses, whereas those who were less avoidant had lower cortisol 6 months postloss. Moreover, poor psychosocial functioning was associated with elevated cortisol only in later (rather than earlier) stages of bereavement (Gerra et al., 2003).

Other bereavement studies document fluctuation in circadian rhythm over the course of a single day; Ong and colleagues (2011) found lower levels of salivary cortisol at awakening, when measured across the day, among bereaved persons who had higher levels of negative emotion. In contrast, a similar study also found that bereaved persons had flatter cortisol patterns over the day compared with nonbereaved; and these effects were more pronounced in widowed people, suggesting that bereaved spouses may be particularly vulnerable (Holland et al., 2013). Although studies show heterogeneity, in particular when cortisol is measured over the day, the evidence generally suggests that those experiencing spousal bereavement evidence higher cortisol levels than nonbereaved controls (Buckley et al., 2009; Khanfer, Lord, & Phillips, 2011).

We propose that the association between spousal loss and cortisol response may operate via specific psychological reactions to loss, where some reactions are associated with higher cortisol levels. For example, emotional numbness, a shock or immobilization response, is a fairly common defense reaction after a spouse's death that can affect cortisol responses (Levy & Sclare, 1976; Parkes, 1998; Maccallum & Bryant, 2011). Emotional numbness that persists for longer than a few weeks may indicate a more problematic grief reaction (Simon et al., 2011). Numbness occurs more often among bereaved people who feel unprepared for their spouses' death (Hauksdóttir, Steineck, Fürst, & Valdimarsdóttir, 2010). If these numbness reactions are prolonged, they can affect HPA responses (Maccallum & Bryant, 2011). Bereavement adjustment is also more difficult after a long, protracted death, especially if extensive caregiving was involved (Sanders, 1982–1983). Consistent with prior work showing men's elevated HPA responses to stress (e.g., Kudielka & Kirschbaum, 2005), we also expect that the effects of numbness, caregiving, and prolongation of death may be larger among men than those among women. Specifically, we anticipate that the associations between spousal loss and loss-related stressors and cortisol reactions will be of significantly greater magnitude among widowers than those among widows.

Drawing upon prior work, we examine the extent to which the context of spousal death (prolongation and caregiving) and specific emotional reactions (emotional numbness) 6 months after the death (W1) are associated with heightened cortisol levels 18 months after the death (W2). We also evaluate whether these effects differ significantly by gender. We use the Changing Lives of Older Couples (CLOC), a prospective multiwave study of late-life spousal bereavement, which obtained detailed assessments of death context and psychological reactions and extensive biomarker data.

Method

Data

CLOC is a prospective study of a two-stage area probability sample of 1,532 married, English-speaking, individuals aged 65+ from the Detroit Standard Metropolitan Statistical Area. No sample members were institutionalized, and all were capable of participating in a 2-hr interview. At baseline, the response rate was 68%, consistent with those obtained in other population-based studies of aging (Carr, Nesse, & Wortman, 2006).

Baseline face-to-face interviews lasting 2 hr were conducted between June 1987 and April 1988. CLOC researchers monitored spousal loss by tracking daily obituaries in three Detroit-area newspapers and using monthly death record tapes provided by the State of Michigan. The National Death Index was used to confirm deaths and obtain causes of death. Of the 335 respondents who lost a spouse during the study period, 316 were contacted for possible interviews (19 persons or 6% had died earlier). Women were oversampled to maximize the number of persons who

would become bereaved during the study, given women's greater likelihood of becoming widowed. Of the 316 contacted, 263 persons (83%) participated in at least one of the three follow-up interviews, conducted at 6 (W1), 18 (W2), and 48 months (W3) after the death of the spouse. The primary reasons for nonresponse were refusal to participate (38%), ill health, or death at follow-up (42%). Data were weighted to take into account unequal probabilities of selection and differential response rates. Weighted sample sizes were 210 widow(er)s (151 women, 59 men) at W1 and 155 widow(er)s (110 women, 45 men) at W2.

Controls from the baseline sample of 1,545 were selected to match the widowed persons along the dimensions of age, race, and sex. The matched controls were re-interviewed at the three follow-up interviews at roughly the same time as their corresponding widowed persons (Carr et al., 2001). The number of control subjects was considerably smaller at the 6-month than the 18-month follow-up. Controls were not available for all bereaved subjects at the 6-month follow-up because funding for the control sample was cut from the proposed budget and was reinstated halfway through the data collection for the 6-month follow-up.

In addition to the face-to-face interviews, randomly selected participants participated in a multiwave biomarker study. Subjects provided urine and blood samples in their homes, which were used to generate multiple biomarker indicators including overnight urinary free cortisol. The biomarker subsample is small but sufficient for adequately powered analyses: 64 widow(er)s at W1 and 61 widow(er)s at W2. These were the same participants although three were lost due to attrition.

Measures

Dependent variable.—Our outcome measure is overnight basal urinary free cortisol, a widely used biological indicator of stress adaptation, collected at W1 and W2. The assessment of urinary cortisol over this period provides a relatively stable indicator of the total cortisol excretion by the adrenal glands and measures the biologically active (unbound) cortisol. Urine samples were provided in the morning, at home, collected by the interviewers, frozen, and then subsequently stored, and analyzed soon after for cortisol levels. The protocol was consistent with procedures from other studies at the time. The unit of measurement for overnight urinary cortisol corrected for creatinine was µg/12 hr, which is consistent with prior studies (e.g., Seeman et al., 2004), including those conducted at the same time as the CLOC in 1988. Further, a 2-year change score of 1.2 µg in urinary cortisol was predictive of negative health outcomes (Seeman, McEwen, Singer, Albert, & Rowe, 1997).

Independent variables.—We focus on three measures of death context found to affect bereavement responses (Carr et al., 2006): emotional numbness, caregiving for the decedent, and duration of death forewarning (all measured at W1). Emotional numbness was measured with the question: "I have a list of feelings and emotions that some people still experience many months after the loss of their husband or wife. During the past month have you felt emotionally numb?" Response categories were as follows: never felt this way, rarely, somewhat, or often. Because 73% of the participants reported no numbness, we recoded responses into 1 = *felt numbness* and 0 = *did not*. Caregiving was assessed retrospectively at W1 with the question: "During the last 6 months of (his/her) life, about how many hours a week did *you* spend providing physical care for your (husband/wife)?" Responses were skewed, with 51.6% reporting that they spent no time caregiving; thus, we dichotomized the measure (1 = *provided care*; 0 = *did not*). Death forewarning was assessed with the question: "How long before your spouse's death did you realize that s/he was going to die?" Open-ended responses were recoded into the categories of no forewarning (40%, reference category); modest forewarning (17%, <1 month); and prolonged forewarning (43%, ≥1 month). Cortisol levels differ by gender and increase with age, so we included gender and age (in years) in our initial analyses. Thus, we considered six independent variables all from W1 (emotional numbness, gave care, some forewarning, prolonged forewarning, age, and gender) and evaluated their associations with both W1 and W2 cortisol levels.

Analysis

First, we examined prospectively changes in cortisol levels from W1 to W2. We conducted a repeated measures analysis of variance (ANOVA) comparing cortisol levels of the same participants (40 widows and 21 matched controls; 24 men and 37 women) at W1 and W2. Then, we examined whether cortisol levels at W1 and W2 varied based on level of emotional numbness, death forewarning, and caregiving reported at W1 by estimating ordinary least squares (OLS) regression. We initially evaluated the effect of numbness and then incorporated indicators of forewarning, caregiving, gender, and age. We included depressive symptoms in our preliminary analyses; the measure was not statistically significant, so we excluded it from our final analyses.

Finally, given that previous researchers have found sex differences in HPA responses to stress, we estimated two-way interaction terms between gender and prolonged forewarning at W1 and between gender and emotional numbness at W2 (see review by Kudielka & Kirschbaum, 2005). A Bonferroni correction was used to account for multiple comparisons. Of the six possible two-way interactions (three two-way interactions for each of the two waves), just one was statistically significant at the $p < .05$ level. The interaction of gender by emotional numbness was significant in models predicting W2 cortisol levels. We present only the model yielding statistically significant effects; all other models are available from the first author.

RESULTS

Descriptive Statistics

The average CLOC participant was aged 70 at baseline (standard deviation [SD] = 6.25; range: 51–86 years), had about 11 years of education, and about 11% were black. Roughly half (48%) were providing care to their spouse prior to loss, and 27% reported feeling emotionally numb in the 6 months immediately following the loss. Mean cortisol levels (controlling for creatinine) at W1 were 14.13 (SD = 10.08) and 17.13 (SD = 15.98) at W2.

Multivariate Analyses

We first evaluated whether bereaved spouses and married matched controls differed significantly in urinary free cortisol at the 6-month and 18-month follow-ups. Based on the repeated measures ANOVA, we observed a significant three-way interaction effect between time, gender, and cortisol, $F(1, 56) = 9.519$, $p < .003$. Among the widowed sample, cortisol levels increased from 9.4 to 15.48 for men but decreased slightly from 15.18 to 13.87 for women between the two waves. Among the control subjects, scores for men decreased slightly from 11.22 to 10.03, whereas scores for women increased sharply from 13.09 to 19.55.

Next, we evaluated the extent to which death circumstances and emotional numbness influenced cortisol levels at W1 and W2. OLS regression results presented in Table 1 show that numbness was not a statistically significant predictor of cortisol at W1, although prolonged forewarning ($\beta = 0.298$) was significant ($p = .03$) in Model 2. When caregiving was added in Model 3, the association between prolonged forewarning and W1 cortisol became nonsignificant; but when control variables were added in Model 4, the association between cortisol and prolonged forewarning emerged as statistically significant ($\beta = 0.308$, $p = .03$). Gender was significantly associated with cortisol levels ($\beta = 0.281$). Bereaved women had higher levels of cortisol than bereaved men at W1. The full model (Model 5) explained 12.2% of the variance. No interaction effects were statistically significant at W1.

In Table 2 (W2 cortisol levels), W1 emotional numbness was a significant predictor ($\beta = 0.510$, $p \leq .001$) in Model 1. Those reporting emotional numbness evidenced higher levels of cortisol at W2. This effect remained statistically significant when age and gender were included in Model 3. An interaction effect between gender and emotional numbness in Model 5 was statistically significant, and the final model explained 31% of the variance. Bereaved men who reported emotional numbness had higher cortisol levels at W2 than bereaved men who did not have these reactions; no significant differences were observed among bereaved women.

DISCUSSION

Our analysis revealed that urinary cortisol levels are associated with the context of spousal bereavement; however, the association differed for widows and widowers. Prolonged forewarning of the death was associated with elevated cortisol levels for both bereaved men and women at W1, yet bereaved men who reported emotional numbness 6 months after spousal loss evidenced higher cortisol levels 18 months postloss (W2), relative to their female counterparts. These findings underscore the importance of considering gender and death context when assessing cortisol levels following the experience of both chronic and acute stressors. Our results are consistent with prior studies showing that adult men respond to psychological stress with greater increases in cortisol compared with adult women and that these reactions are moderated by the type of stressor (Kudielka & Kirschbaum, 2005). For example, we found that while prolonged forewarning suppressed cortisol recovery for widows and widowers in general, bereaved men who felt emotional numbness soon after spousal loss evidenced significantly higher cortisol levels several months postloss, compared with bereaved women who also had experienced emotional numbness.

Although Ong and colleagues (2011) observed that bereaved persons have flatter diurnal cortisol slopes across the day than nonbereaved persons, our analysis reveals that high urinary cortisol levels are associated with particular circumstances of spousal bereavement and emotional

Table 1. Hierarchical Regression Predicting W1 Cortisol (N = 64) Bereaved Only

	Model 1	Model 2	Model 3	Model 4	Model 5
	B SE(B), β	B SE(B), β	B SE(B), β	B SE(B), β	B SE(B), β
W1 numbness	−0.870 (4.27) −0.026	−1.00 (4.16) −0.030	−1.48 (4.25) −0.044	−2.59 (4.24) −0.077	−2.59 (4.18) −0.077
W1 some forewarning		5.98 (4.51) 0.176	5.58 (4.58) 0.164	4.72 (4.56) 0.139	5.12 (4.51) 0.151
W1 prolonged forewarning		7.31 (3.26) 0.298*	6.55 (3.50) 0.267	7.57 (3.46) 0.308*	−11.7 (12.55) −0.478
W1 gave care (1 = yes)			2.01 (3.31) 0.084	−0.245 (3.35) −0.010	0.236 (3.32) 0.010
W1 age (age in years)				−0.174 (0.272) −0.089	0.037 (0.299) 0.019
W1 gender (1 = female)				7.36 (3.66) 0.281*	3.35 (4.40) 0.128
W1 Gender × Prolonged					11.3 (7.07) 0.819
Adjusted R^2	−0.016	0.037	0.027	0.098	0.122

Notes. B = unstandardized beta; β = standardized beta; SE = standard error.
***p < .001, **p < .01, *p < .05.

Table 2. Hierarchical Regression Predicting W2 Cortisol (*N* = 61) Bereaved Only

	Model 1	Model 2	Model 3	Model 4	Model 5
	B (SE B) β	*B (SE B)* β	*B (SE B)* β	*B (SE B)* β	*B (SE B)* β
W1 numbness	22.2 (4.87) 0.510***	20.0 (5.00) 0.459***	19.8 (5.08) 0.455***	19.8 (5.12) 0.454***	66.63 (18.60) 1.529***
W1 some forewarning		−0.605 (5.60) −0.013	−0.713(5.66) −0.015	0.682 (5.84) 0.015	−0.605 (5.58) −0.013
W1 prolonged forewarning		6.83 (4.51) 0.190	6.13 (5.12) 0.171	6.10 (5.22) 0.170	5.01 (4.97) 0.140
W1 gave care (1 = yes)			1.37 (4.65) 0.038	1.64 (4.94) 0.046	−1.21 (4.82) −0.034
W1 age (in years)				−.230 (.36) −0.076	−0.279 (.35) −0.092
W1 gender (1 = female)				−4.54 (4.54) −0.126	1.34 (4.90) 0.036
W1 Gender × Numbness					−27.33 (10.47) −1.106**
Adjusted R^2	0.247	0.259	0.247	0.237	0.310

Notes. B = unstandardized beta; β = standardized beta; *SE* = standard error.
***p < .001, **p < .01, *p <. 05.

reactions to the loss. (Cortisol has a circadian cycle with levels highest in the morning and declines thereafter across the day; individuals who do not show linear declines across the day, i.e., a flatter slope, are more vulnerable to disease.) Importantly, however, both indices (i.e., flat cortisol slopes across the day and high basal levels of urinary cortisol) are associated with negative health outcomes in the long term (Michaud et al., 2008; Vogelzangs et al., 2010).

Our data are also consistent with previous research showing that psychological reactions and circumstances related to the stressor of spousal bereavement are linked to cortisol changes among older adults (Gerra et al., 2003). Widow(er)s in the CLOC, who experienced prolonged forewarning, had higher cortisol levels at W1 postbereavement than those whose spouses died suddenly. Studies focusing on self-reported psychological outcomes also reveal that adjustment to loss varies based on the death context, including the duration of forewarning (e.g., Carr et al., 2001). Our findings underscore the importance of focusing on specific stressors when examining bereaved persons' cortisol reactions.

The association between W1 emotional numbness and W2 cortisol levels are consistent with the work of Gerra et al. (2003), showing that emotional numbness is related to cortisol levels for up to 18 months after bereavement. Previous studies suggesting that emotional numbness is associated with lack of preparedness for a spouse's death, especially among bereaved men, are also consistent with our results (e.g., Hauksdóttir et al., 2010). Hauksdóttir and colleagues found that widowers who felt unprepared for their wives' deaths demonstrated more emotional numbness, shock, and heightened anxiety than widowers who expected the death. These widowers also evidenced an elevated risk of complicated grief reactions several months after bereavement, a prolonged reaction that was not evident among the more prepared widowers. Our results corroborate this study and show that such patterns are limited to men only.

Gender differences in reactions to bereavement have been found in previous research, with most finding that older widowers adjust more slowly than older widows (Schut, Stroebe, van den Bout, & de Keijser, 1997). Our

findings revealed comparable differences in cortisol response. In particular, our results are consistent with the work of Kudielka and Kirschbaum (2005), showing that older women typically evidence higher cortisol levels than older men, but bereaved men who initially respond to the loss of a spouse with shock or emotional numbness are more likely than older bereaved women to show higher cortisol levels. Kudielka and Kirschbaum (2005) also caution that the reasons underlying these gender differences in stress reactivity remain unclear. A larger sample is necessary for more in-depth analyses of the differences in men's and women's cortisol responses after bereavement.

Taken together, our results underscore the need to examine more fully and systematically the circumstances surrounding bereavement, in light of emerging research reporting complex associations among life stressors, cortisol, and later life health. Chronic strains associated with prolonged forewarning of an impending death of spouse are associated with stress-related neuroendocrine reactions for longer durations than previously documented, which may affect health and longevity. However, these associations may vary based on other personal characteristics, especially gender and one's own baseline physical and emotional health. Our study is the first to demonstrate a link between the circumstances surrounding a spouse's death and cortisol levels of older widows and widowers.

Limitations and Future Directions

Our research suggests that the circumstances surrounding bereavement are associated with prolonged and heightened cortisol levels among older widow(er)s. However, our study has several weaknesses that may limit its generalizability. Our sample is small and focuses on a single cohort of widow(er)s residing in one region of the United States. We encourage others to replicate our analyses using larger, more recent, and more heterogeneous samples. Given our small sample, we included only a few carefully selected controls. We did not consider specific health conditions such as blood pressure or health behaviors such as diet and exercise, which have been found to affect cortisol levels (Chida & Steptoe, 2009). However, some scholars have

argued that there is often overcorrection for potential confounds in biobehavioral research when using small samples (Segerstrom, 2009). Future studies also should consider a broader range of death-context factors, including a more fine-grained measure of caregiving, such as perceived intrusiveness or stressfulness.

Although we documented an association between spousal death and cortisol levels, we did not identify the specific psychological or biological pathways accounting for the association. We did not explore the consequences of elevated cortisol levels for subsequent health outcomes, such as mortality risk. Finally, our measures of cortisol are potentially problematic. We could not examine preloss levels of cortisol because the baseline measures were lost due to a refrigeration problem, and details regarding the transport of urine to the laboratory are unavailable. However, the CLOC's collection of multiwave data from widow(er)s allows us to study cortisol at two points postloss, even if we cannot track within-person change preloss and postloss.

Despite these limitations, we have demonstrated the linkage between spousal death context and cortisol at W1 and W2, the specific psychosocial factors associated with cortisol responses during bereavement, and gender differences therein. Finally, our study highlights the value of adopting an integrative, biopsychosocial approach to exploring the complex interplay among psychological factors, stress-related reactions, and immune responses.

References

Bennett, K. M. (2006). Does marital status and marital status change predict physical health in older adults? *Psychological Medicine*, *36*, 1313–1320. doi:10.1017/S003329170600818X

Buckley, T., Bartrop, R., McKinley, S., Ward, C., Bramwell, M., Roche, D., … Tofler, G. H. (2009). Prospective study of early bereavement on psychological and behavioural cardiac risk factors. *Internal Medicine Journal*, *39*, 370–378. doi:10.1111/j.1445-5994.2008.01879.x

Buckley, T., McKinley, S., Tofler, G., & Bartrop, R. (2010). Cardiovascular risk in early bereavement: A literature review and proposed mechanisms. *International Journal of Nursing Studies*, *47*, 229–238. doi:10.1016/j.ijnurstu.2009.06.010

Carr, D., House, J. S., Wortman, C., Nesse, R., & Kessler, R. C. (2001). Psychological adjustment to sudden and anticipated spousal loss among older widowed persons. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, *56*, S237–S248. doi:10.1093/geronb/56.4.S237

Carr, D., Nesse, R., & Wortman, C. B. (Eds.). (2006). *Spousal bereavement in late life*. New York: Springer.

Chida, Y., & Steptoe, A. (2009). Cortisol awakening response and psychosocial factors: A systematic review and meta-analysis. *Biological Psychology*, *80*, 265–278. doi:10.1016/j.biopsycho.2008.10.004

Cleare, A. J., Blair, D., Chambers, S., & Wessely, S. (2001). Urinary free cortisol in chronic fatigue syndrome. *American Journal of Psychiatry*, *158*, 641–643. doi:10.1176/appi.ajp.158.4.641

Epel, E. S., Burke, H. M., & Wolkowitz, O. M. (2007). The psychoneuroendocrinology of aging: Anabolic and catabolic hormones. In C. M. Aldwin, C. L. Park, & A. Spiro III (Eds.). *Handbook of health psychology and aging* (pp. 119–141). New York: The Guilford Press.

Gerra, G., Monti, D., Panerai, A. E., Sacerdote, P., Anderlini, R., Avanzini, P., … Franceschi, C. (2003). Long-term immune-endocrine effects of bereavement: Relationships with anxiety levels and mood. *Psychiatry Research*, *121*, 145–158. doi:10.1016/S0165-1781(03)00255-5

Glaser, R., & Kiecolt-Glaser, J. K. (2005). Stress-induced immune dysfunction: Implications for health. *Nature Reviews. Immunology*, *5*, 243–251. doi:10.1038/nri1571

Hauksdóttir, A., Steineck, G., Fürst, C. J., & Valdimarsdóttir, U. (2010). Long-term harm of low preparedness for a wife's death from cancer—A population-based study of widowers 4-5 years after the loss. *American Journal of Epidemiology*, *172*, 389–396. doi:10.1093/aje/kwq147

Holland, J. M., Rozalski, V., Thompson, K. L., Tiongson, R. J., Schatzberg, A. F., O'Hara, R., & Gallagher-Thompson, D. (2013). The unique impact of late-life bereavement and prolonged grief on diurnal cortisol. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*. Advance online publication on June 5, 2013. doi:10.1093/geronb/gbt051

Irwin, M., Daniels, M., Risch, S. C., Bloom, E., & Weiner, H. (1988). Plasma cortisol and natural killer cell activity during bereavement. *Biological Psychiatry*, *24*, 173–178. doi:10.1016/0006-3223(88)90272-7

Khanfer, R., Lord, J. M., & Phillips, A. C. (2011). Neutrophil function and cortisol: DHEAS ratio in bereaved older adults. *Brain, Behavior, and Immunity*, *25*, 1182–1186. doi:10.1016/j.bbi.2011.03.008

Kudielka, B. M., & Kirschbaum, C. (2005). Sex differences in HPA axis responses to stress: A review. *Biological Psychology*, *69*, 113–132. doi:10.1016/j.biopsycho.2004.11.009

Levy, B. & Sclare, A. B. (1976). A study of bereavement in general practice. *Journal of the Royal College of General Practitioners*, *26*, 329–336.

Maccallum, F., & Bryant, R. A. (2011). Imagining the future in complicated grief. *Depression and Anxiety*, *28*, 658–665. doi:10.1002/da.20866

McEwen, B. S. (2003). Mood disorders and allostatic load. *Biological Psychiatry*, *54*, 200–207. doi:10.1016/S0006-3223(03)00177-X

Michaud, K., Matheson, K., Kelly, O., & Anisman, H. (2008). Impact of stressors in a natural context on release of cortisol in healthy adult humans: A meta-analysis. *Stress (Amsterdam, Netherlands)*, *11*, 177–197. doi:10.1080/10253890701727874

Ong, A. D., Fuller-Rowell, T. E., Bonanno, G. A., & Almeida, D. M. (2011). Spousal loss predicts alterations in diurnal cortisol activity through prospective changes in positive emotion. *Health Psychology*, *30*, 220–227. doi:10.1037/a0022262

Otte, C., Hart, S., Neylan, T. C., Marmar, C. R., Yaffe, K., & Mohr, D. C. (2005). A meta-analysis of cortisol response to challenge in human aging: Importance of gender. *Psychoneuroendocrinology*, *30*, 80–91. doi:10.1016/j.psyneuen.2004.06.002

Parkes, C. M. (1998). Coping with loss: Bereavement in adult life. *British Medical Journal*, *316*, 856. doi:10.1136/bmj.316.7134.856

Piazza, J. R., Almeida, D. M., Dmitrieva, N. O., & Klein, L. C. (2010). Frontiers in the use of biomarkers of health in research on stress and aging. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, *65*, 513–525. doi:10.1093/geronb/gbq049

Roy, A., Gallucci, W., Avgerinos, P., Linnoila, M., & Gold, P. (1988). The CRH stimulation test in bereaved subjects with and without accompanying depression. *Psychiatry Research*, *25*, 145–156. doi:10.1016/0165-1781(88)90045-5

Sanders, C. M. (1982–1983). Effects of sudden vs. chronic illness on bereavement outcome. *Omega*, *13*, 217–232. doi:10.2190/RTPF-M5EA-6N7A-7D0D

Schut, H. A., Stroebe, M. S., van den Bout, J., & de Keijser, J. (1997). Intervention for the bereaved: Gender differences in the efficacy of two counselling programmes. *British Journal of Clinical Psychology/British Psychological Society*, *36* (Pt 1), 63–72. doi:10.1111/j.2044–8260.1997.tb01231.x

Seeman, T. E., Crimmins, E., Huang, M. H., Singer, B., Bucur, A., Gruenewald, T., … Reuben, D. B. (2004). Cumulative biological risk and socio-economic differences in mortality: MacArthur studies of successful aging. *Social Science & Medicine (1982)*, *58*, 1985–1997. doi:10.1016/S0277-9536(03)00402-7

Seeman, T. E., McEwen, B. S., Singer, B. H., Albert, M. S., & Rowe, J. W. (1997). Increase in urinary cortisol excretion and memory declines: MacArthur studies of successful aging. *Journal of Clinical Endocrinology and Metabolism*, *82*, 2458–2465. doi:10.1210/jc.82.8.2458

Segerstrom, S. C. (2009). Biobehavioral controls: Threats to psychoneuro-immunology research? *Brain, Behavior, and Immunity*, *23*, 885–886. doi:10.1016/j.bbi.2009.05.053

Simon, N. M., Wall, M. M., Keshaviah, A., Dryman, M. T., LeBlanc, N. J., & Shear, M. K. (2011). Informing the symptom profile of complicated grief. *Depression and Anxiety*, *28*, 118–126. doi:10.1002/da.20775

Spratt, M. L., & Denney, D. R. (1991). Immune variables, depression, and plasma cortisol over time in suddenly bereaved parents. *Journal of Neuropsychiatry and Clinical Neurosciences*, *3*, 299–306.

Van Cauter, E., Leproult, R., & Kupfer, D. J. (1996). Effects of gender and age on the levels and circadian rhythmicity of plasma cortisol. *Journal of Clinical Endocrinology and Metabolism*, *81*, 2468–2473. doi:10.1210/jc.81.7.2468

Vogelzangs, N., Beekman, A. T., Milaneschi, Y., Bandinelli, S., Ferrucci, L., & Penninx, B. W. (2010). Urinary cortisol and six-year risk of all-cause and cardiovascular mortality. *Journal of Clinical Endocrinology and Metabolism*, *95*, 4959–4964. doi:10.1210/jc.2010-0192

Williams, K. (2004). The transition to widowhood and the social regulation of health: Consequences for health and health risk behaviors. *Journals of Gerontology, Series B: Psychological Sciences and Social Sciences*, *59*, 343–349. doi:10.1093/geronb/59.6.S343