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Aging and the HPA axis: Stress and resilience in older adults

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Abstract

Hypothalamic-pituitary-adrenal (HPA) axis function may change over the course of aging, and altered diurnal or stress-induced secretion of the hormone cortisol could predispose older adults to negative health outcomes. We propose that psychological resilience may interact with diurnal cortisol to affect health outcomes later in life. Emotion regulation and social support are two constructs that contribute to resilience and exhibit age-specific patterns in older adults. Determining how the use of resilience resources interacts with age-related diurnal cortisol will improve our understanding of the pathways between stress, resilience, and well-being. In this review, we assess published studies evaluating diurnal cortisol in older adults to better understand differences in their HPA axis functioning. Evidence thus far suggests that diurnal cortisol may increase with age, although cross-sectional studies limit the conclusions that can be drawn. We also review extant evidence connecting age-specific signatures of emotion regulation and social support with diurnal cortisol. Conclusions are used to propose a preliminary model demonstrating how resilience resources may modulate the effects of cortisol on health in aging.

Keywords

Lifespan; Human; Stress; HPA axis; Resilience; Cortisol; Emotion; Emotion regulation; Social support

1. Introduction

1.1. Later life stress, resilience and health

Between now and 2050, the United States is projected to experience rapid growth in its older adult population relative to other age groups.[1] The shift is attributable to the increasing number of “Baby Boomers” joining those ranks (United States Census Bureau, 2010) and to lower birth rates (Population Reference Bureau, 2012). To promote the well-being of this burgeoning group, and to increase our overall understanding of aging, it is timely to evaluate factors that affect older adults’ psychobiological responses to stress, resilience to stress, and subsequent effects on health. Older adults’ experience of acute and chronic stress is similar to that faced earlier in the lifespan. In general, acute stress involves a specific and usually uncontrollable life event, and the accompanying perceived emotional and/or physiological

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[1]The older population has been defined as adults who are aged 60 years and above (World Health Organization, 2013).

challenge (e.g., giving a speech while being evaluated/judged; Dickerson and Kemeny, 2004). Older adults commonly experience acute stress due to mental and physical decline, which can develop into chronic stress. Chronic stress is an individual's response to a stressor that persists over a prolonged period of time (e.g., caregiving; Miller et al., 2007) or to repeated acute stressors (e.g., negative interpersonal experiences; Rosnick et al., 2007; Uchino et al., 2001). Older adults are more likely to endure certain chronic psychosocial stressors—specifically, bereavement and spousal caregiving (Moss et al., 2001; Ong et al., 2006). This review primarily focuses on older adults' responses to chronic stress.

The hypothalamic-pituitary-adrenal (HPA) axis is a primary stress system in the human body, one that we share with all vertebrate animals. The system is subject to diurnal variation and is also sensitive to both acute and chronic stress. Therefore, the HPA axis is important for understanding resilience to stress. *Psychological resilience* (hereafter, termed simply "resilience") may help to buffer against the effects of age-associated chronic stress on the HPA axis. Resilience is viewed as a state/process construct (Montpetit et al., 2010) as well as a trait construct (Bartone et al., 1989; Bergeman and Deboeck, 2014). In general, *resilience* has been defined as the ability to "bounce back" from adversity (Block and Kremen, 1996) to resist, cope with, recover from, and succeed in the face of adverse life experiences (Masten and Powell, 2003), and to see difficulties as challenges to be mastered rather than threats to be endured (Kobasa and Puccetti, 1983).

Although resilience can also be conceptualized as the strength and benefits obtained from coping successfully with a trauma or stressor, for the purposes of this review, we conceptualize resilience as the extent to which individuals' coping mechanisms buffer against stress, prior to or during stress. Resilience can also fluctuate due to changes in perceived stress or in physical or environmental factors, such as those that occur later in life (Bergeman and Wallace, 1999; Garmezy, 1985; Rutter, 1987). Emotion regulation and social support are two primary factors that contribute to resilience (Ong et al., 2009; Fredrickson et al., 2003; Tugade et al., 2004), which is conceptualized in this review as a separate construct from these contributing factors. Resilience also reflects other state and trait psychosocial resources (e.g., hardiness; Kobasa and Puccetti, 1983) not described here. But how does resilience promote health and well-being? The HPA axis represents one key pathway; as indicated above, the system is activated during stress and may also be central to resilience.

1.2. The HPA axis and stress in older adults

In response to challenge or threat, the HPA system produces a cascade of hormones, resulting in the secretion of glucocorticoids (GCs), most importantly cortisol. In the absence of an identifiable stressor, cortisol is secreted over a 24-h period according to daily (i.e., diurnal) fluctuations (Otte et al., 2005). Cortisol levels vary according to a person's wake-sleep cycles and exposure to light-dark cycles, as well as from the endogenously generated circadian rhythm (Van Cauter, 1990). Thus, circulating cortisol levels change due to both environmental and endogenous influences. Studies of individuals' basal (i.e., unmanipulated/unstressed) diurnal-cortisol secretion provide an important index of HPA axis activity.

The HPA axis contains a negative-feedback mechanism designed to regulate GC levels. Through negative feedback, GCs essentially "turn off" their own secretion, by down-

regulating release of the hormones (corticotropin-releasing hormone [CRH] and adrenocorticotropic hormone [ACTH]) that cause production of GCs. In other words, an increase in cortisol causes a decrease in the release of CRH and ACTH and eventually down-regulates the HPA axis to a pre-stress baseline. However, negative feedback may be more or less effective in different individuals. A person's degree of negative feedback is influenced by their sensitivity to GCs, which in turn is determined by number of glucocorticoid receptors (GRs) present in the brain as well as how accessible one's GRs are, which is influenced by a number of cellular processes.

HPA axis dysregulation can theoretically be achieved through several pathways. It may begin with chronic stress causing prolonged high activity in the HPA axis. Prolonged exposure to high GC levels might lead to decreased GR sensitivity in the brain, which would result in less negative feedback, since negative feedback relies on GR to hear the cortisol "signal" (Becker et al., 2002; Nelson, 2005). Impaired negative feedback could even lead to further long-term elevations in cortisol, prolonging the cycle (Sapolsky et al., 1986). A second pathway may begin with individuals that have fewer GR or less GR accessibility for any number of reasons, be it from genetic causes, early life experiences (Szyf et al., 2005), ongoing stressors causing short-term changes (Rohleder et al., 2003), etc. Fewer or less accessible GRs could produce lower negative feedback, which then could lead to high cortisol, as discussed above. Importantly, however, chronic stress has been associated with both high *and* low GC levels (hypercortisolism or hypocortisolism, respectively; see Miller et al., 2007 for a meta-analysis of chronic stress and the HPA axis, and Rohleder et al., 2010 for discussion of possible mechanisms). GC levels may reflect the effects of chronic stressors such as financial hardship, work overload, and burnout (Wirth and Gaffey, 2013). Furthermore, the HPA axis is closely tied with the body's immune, nervous, and other endocrine systems (Maier and Watkins, 1998; Stratakis and Chrousos, 1995; Toufexis et al., 2014). Therefore, the HPA response and inactivation are both directly and indirectly central to health.

In the general population, disturbances in HPA axis regulation and/or chronic stress have been correlated with negative health outcomes such as a higher risk for mood, anxiety, and stress-related disorders (e.g., Djernes, 2006; Hammen, 2005; Slavich and Irwin, 2014; Vreeburg et al., 2010; Yehuda, 2006), cardiovascular disease and hypertension (Go et al., 2013; Kivimäki et al., 2006; Krantz and McCeney, 2002), rheumatoid arthritis (de Brouwer et al., 2014; Straub et al., 2005), decreased immunity (Epel et al., 2004; Gouin et al., 2008), greater hospitalization and risk of mortality in patients with chronic obstructive pulmonary disease (Clark et al., 2015), and faster progression of cancer and HIV/AIDS (Antoni et al., 2006; Leserman, 2000). Of relevance to this review, in older adults, greater diurnal cortisol secretion has been associated with frailty (Johar et al., 2014), whereas lower diurnal cortisol is correlated with longevity (Noordam et al., 2012). More specifically, altered morning-cortisol levels (i.e., the cortisol awakening response [CAR]; Fries, et al., 2009) or a flatter morning-to-evening diurnal cortisol slope (Adam et al., 2006) may signify HPA dysregulation. In older adults, a lower CAR has been reported in those with generalized anxiety disorder (Hek et al., 2013). In another example, a flatter diurnal profile has been connected with Type 2 Diabetes (Hackett et al., 2014) and earlier mortality in younger and older adult cancer patients (Sephton et al., 2000). The connections between aging and these

more nuanced measures of HPA axis activity, such as CAR and diurnal cortisol slope, are discussed later in this paper.

Causality is difficult to determine from existing studies of cortisol and health, most of which are correlational in nature. However, if there are age-induced changes in HPA axis activity, such as increased diurnal cortisol secretion as people age, then those changes could critically affect older adults' health. In other words, if it is true that diurnal cortisol levels change significantly with aging, this could have serious clinical implications for the older population (for reviews, see Conrad and Bimonte-Nelson, 2010; Magri et al., 2006; Murri et al., 2014). Furthermore, there are many trajectories of aging. First, there is "normal" aging, when people are relatively healthy although their health declines over time. Second, there are very healthy "thrivers," who may not be representative of the greater population. And third, there are individuals who become very ill as they age. HPA axis changes (or the lack of change) could differ during each aging trajectory.

In addition to requiring more information about age-related changes in the HPA axis, scholars have called for a greater inclusion of biological factors into research examining adults' resilience (Curtis and Cicchetti, 2003; Lavretsky and Irwin, 2007). Resilience resources of emotion regulation and social support have been studied in conjunction with adults' diurnal cortisol (e.g., Adam et al., 2006; Lai et al., 2012) and may protect or enhance effects of altered HPA axis functioning on health. For example, certain patterns of HPA axis activity (e.g., higher diurnal cortisol), combined with lower resilience resources (e.g., poor social support), could jointly predispose individuals to psychophysiological consequences or have greater consequences for patients with chronic illness. The older adult population is already at an increased risk for a number of chronic health conditions (e.g., diabetes, heart disease, high blood pressure) that are common later in life (AARP Public Policy Institute, 2009). Examining older adults' HPA axis functioning is a fruitful direction to pursue in order to better understand health outcomes in older age, as well as how resilience affects the HPA axis.

1.3. Aims of the review

As mentioned previously, older adults are a growing proportion of the U.S. population (Population Reference Bureau, 2012; United States Census Bureau, 2010). Although older age is associated with less frequent daily stressors (Stawski et al., 2013), a lifetime of enduring the physiological effects of stress, chronic stress in later life, and normal biological aging could all contribute to age differences in HPA axis activity and enhance susceptibility to health problems (e.g., Abercrombie, 2009; Lupien and McEwen, 1997; Vreeburg et al., 2010; Wolf, 2003). However, as mentioned earlier, there is little evidence regarding how the HPA axis changes with age (Luthar et al., 2000; Ong et al., 2009). The overarching aim of this paper is to review older adults' diurnal cortisol patterns to increase our understanding of HPA axis aging in this group.

The first specific objective of this review is to better understand age differences in HPA axis activity by evaluating studies examining age effects on trait levels of diurnal cortisol, taking into consideration the strengths and limitations of those studies. Older adults' resilience may help to buffer against age differences in HPA functioning. Thus, our second specific

objective is to determine the extent to which older adults' use of emotion regulation and social support are associated with different patterns of trait diurnal cortisol. Our final specific objective is to integrate conclusions from cortisol, emotion regulation, and social support research to construct a preliminary model of aging, stress and resilience. Unifying this literature will improve our understanding of whether the HPA axis changes with age and how older adults' biological and psychosocial profiles may together affect resilience; will assist in developing prescriptions for future research in older cohorts; and will further our knowledge of resilience to stress and health across the spectrum of human development.

2. HPA axis activity in older adults

2.1. Diurnal cortisol assessment

To understand resilience more fully, it is first necessary to establish how the HPA axis changes as people age. Investigators have addressed this question by measuring age-cohort differences in cortisol secretion across an entire day (i.e., diurnal cortisol). Diurnal cortisol is a reliable, proximal index of basal HPA axis activity. Cortisol's diurnal rhythm follows a distinct pattern: The hormone typically rises in the early morning and decreases throughout the rest of the day, reaching a nadir around midnight (Fries et al., 2009). As noted earlier, patterns of diurnal cortisol can change due to long-term exposure to stress. For example, unemployed versus employed individuals exhibit higher morning cortisol and lower evening cortisol (Ockenfels et al., 1995). Thus, cortisol's diurnal pattern is valuable for assessing physiological changes associated with chronic stress.

Researchers use several indices to capture cortisol's diurnal rhythm. One way to summarize multiple cortisol measurements is to calculate area under the curve (AUC), based on the change in cortisol over multiple time points (Pruessner et al., 2003). There are two methods for calculating AUC: AUC with respect to increase (AUCi) approximates *the net change in hormonal levels beyond a baseline* across a given timeframe, and AUC with respect to ground (AUCg), which captures *total hormonal output* across a timeframe (Pruessner et al., 2003). Other indices used to operationalize diurnal cortisol levels include decline or slope (from morning wake to bedtime); mean cortisol across the samples collected; the peak and nadir of the daily rhythm; and the cortisol awakening response (CAR), which can be expressed as an AUC, or as a difference score from wake to peak.

The CAR is a distinct neuroendocrine phenomenon, over and above cortisol's endogenously generated circadian rise (Wilhelm et al., 2007). After waking on a typical morning, cortisol increases 50%–150% for approximately 30–45 min (Fries et al., 2009). Importantly, the CAR is driven by *morning awakening*, and does not occur in response to waking during other times of the day, such as after naps (Federenko et al., 2004). The CAR's precise biological function is unknown, but may pertain to anticipation of the day and mobilization of energy for the day, in relation to stored information that is accessed as a person becomes conscious (Fries et al., 2009). Alterations in the CAR are associated with a variety of adverse health conditions (see Fries et al., 2009 for a review). The CAR may also become altered due to chronic stress (e.g., Schlotz et al., 2004; Wust et al., 2000). Thus, the CAR is another important variable for assessing age-related changes in diurnal cortisol.

A growing body of literature indicates that diurnal cortisol levels may change with age, but findings are inconsistent. Although it is important to consider age-related changes in the HPA axis in a more nuanced way (e.g., assessing the CAR), the basic associations between age and HPA activity are not well researched and must be outlined first. Broadly, does diurnal cortisol increase or decrease with age? Variously, researchers have concluded that cortisol levels: (a) *decline with age* (e.g., Brandtstädter et al., 1991; Evans et al., 2011; Heaney et al., 2010, 2012), (b) *are uncorrelated with age* (e.g., Hansen et al., 2003; Lederbogen et al., 2010; Lupien et al., 1996; Pruessner et al., 1997a,b), or (c) *increase with age* (e.g., Bergendahl et al., 2000; Dmitrieva et al., 2013; Karlamangla et al., 2013; Laughlin and Barrett-Connor, 2000; Nater et al., 2013). Within this body of research, some studies have investigated more specific measures of diurnal cortisol (e.g., slope; Nater et al., 2013), but additional work is required to examine these associations in a more nuanced way.

2.1.1. Methodological problems in diurnal cortisol studies—Contradictory age–cortisol findings may result from methodological flaws, which call into question the validity of those results. First, researchers have often obtained too few cortisol samples (Clow et al., 2004; Nater et al., 2013). There is significant within-person variability in individuals' hormone levels both during a given day and across several days (Almeida et al., 2009a). Cortisol fluctuates due to changing metabolic demands, such as exercise or eating, which need to be controlled behaviorally or statistically. Cortisol also fluctuates due to emotional and situational factors, such as stress experienced during a workday versus the weekend (Van Eck and Nicolson, 1994). Most studies examining age effects on cortisol have collected samples on a single day, used too few daily collection time-points, or restricted sample collection to one part of the diurnal cycle. To examine the diurnal rhythm comprehensively, samples must be collected over many days to create measures of more stable, trait-like cortisol levels (Hellhammer et al., 2007; Pruessner et al., 1997a,b). Relatedly, studies using different statistical methods to calculate overall output, the CAR, or diurnal slope also make comparing the aging-cortisol results problematic.

When collecting diurnal cortisol data, researchers must maintain consistent (within and across participants) and accurate sample timing; the diurnal pattern in cortisol means that samples from very different times of day cannot be compared to each other. Instead of depending on participants' self-report of collection times, some studies have used electronic monitoring devices (e.g., MEMS track caps and smart boxes), which record when samples are deposited. However, as researchers cannot determine the amount of time between individuals' actual awakening and when they provide their initial sample, these methods do not ensure compliance with collection procedures (Dockray et al., 2008). Other research teams have used more objective monitoring approaches (i.e., electrocardiography, polysomnography, or actigraphy) to assess compliance with the timing of a waking sample (see Stalder et al., 2016 for CAR measurement guidelines). To date, no known study of healthy older adults' diurnal cortisol that collected multiple samples has used those monitoring approaches. Other methodological flaws include not controlling for variables that affect HPA axis activity (such as smoking, food and caffeine intake, and vigorous exercise) and small samples sizes (Clow et al., 2004). Too small a sample size can render a study unlikely to have sufficient statistical power to detect true effects in hormone measures

(Almeida et al., 2009a), which have notoriously high variability (Pruessner et al., 1997a,b). Thus, investigators examining smaller sample sizes have an increased risk of making a Type 1 error, rendering potentially spurious findings. Moreover, effect sizes are usually not reported, further limiting the interpretation of studies examining diurnal cortisol fluctuations.

Discrepancies between results may also reflect studies' varying sociodemographic characteristics related to participants' age range or sex. Some cortisol and aging studies have included individuals older than 80 years of age (e.g., Carvalhaes-Neto et al., 2003; Sharma et al., 1989; Vermeulen et al., 1982). Yet those individuals may experience greater decline and developmental losses compared to adults in the 60–80-year-old range (Heckhausen et al., 1989); moreover, age, chronic stress, and cortisol associations may be markedly different in the oldest adults. Sex differences should also be accounted for, in part because women have a longer life expectancy than men (Xu et al., 2014), an effect that likely stems from both physiological and psychosocial factors. Thus, if studies examining older individuals include disproportionate numbers of women, sex and age could become confounded. Overall, examining a broader adult sample may help to determine not only whether, but also, when changes in the age-cortisol association occur during the lifespan (Almeida and Wong, 2009).

2.1.2. Studies with comprehensive cortisol assessment—To begin to resolve how age affects diurnal cortisol, we identified all previous investigations of the association between age and diurnal cortisol or the CAR in saliva or plasma. We located articles published in the English language by searching Google Scholar, PsycInfo, and PubMed using combinations of keywords including adult, older adult, elderly, cortisol, diurnal cortisol, glucocorticoids, HPA axis, aged, aging, geriatric, adult, adulthood, and human. The final search was conducted in March 2016. The reviewed studies were limited to those that examined healthy adults and used a more optimum cortisol-sampling methodology: collecting morning and evening cortisol samples a minimum of three times per day, on at least three days. To be comprehensive, we did not exclude studies based on other methodological flaws (e.g., using a restrictive or overly inclusive age range; sampling a disproportionate number of men versus women). Even so, only five studies met these criteria, all of which assessed cortisol in saliva. Participant demographic and methodological information relevant to assessing cortisol is detailed in Table 1.[2]

Almeida et al. (2009b) examined men and women participating in the National Study of Daily Experiences (NSDE), a sub-section of the National Study of Midlife Development in the United States (MIDUS). Men displayed a significantly greater CAR with older age, but age effects were not significant for women. Older men (>69 years old) also demonstrated greater between-day variability in CAR levels compared to younger men (aged < 45 years old). In contrast, CAR variability was comparable in older and younger women. These findings highlight how the magnitude of the CAR and daily CAR variability may vary by sex as well as by age. The authors suggest that the observed effects of sex may be associated

[2]As a caveat, these studies used similar—but not identical—statistical methods to determine cortisol's diurnal trajectory and slope, making comparison of the results challenging. On the other hand, the studies' cortisol sampling is methodologically rigorous such that, when taken together, the findings provide some clues about how diurnal cortisol changes with age.

with different levels of daily stress faced by women when preparing to meet greater daily social challenges (e.g., as a caregiver), resulting in more weekday to weekend CAR variability. In turn, they suggest that men's daily challenges (and CAR variability) increase with age, although women's challenges remain consistent during aging. Alternately, it is possible that women's lower recorded sampling-collection compliance obscured similar age effects in women as those reported for men.

In a different study that also examined NSDE data (Karlamangla et al., 2013), men and women were categorized into three groups of comparable size: <50 years, 50–64 years, and 65+ years. Age and male sex were each independently associated with a higher diurnal cortisol peak, nadir, and overall output (i.e. AUCg). When collapsed across sex, the oldest group had significantly higher waking cortisol, peak, nadir, and output, compared to the middle-aged and younger adult groups. Regardless of age group, men exhibited a higher nadir and AUCg than women. Interestingly, despite significant differences in the overall values of the cortisol peak and nadir, the daily timing of those events was consistent across age and sex. This observation suggests that the timing of the diurnal pattern is preserved in older age, even if cortisol output may increase. Karlamangla et al. (2013) contended that if cortisol's damaging effects occur from maintained elevations, then AUCg and nadir cortisol indices could be more predictive of health than slope. Importantly, though, other ways of representing cortisol output, such as diurnal slope and CAR, have predicted meaningful outcomes. An altered CAR and/or flattened slopes have been connected with a number of adverse health conditions (e.g., Kumari et al., 2009, 2010a,b; Nater et al., 2008; Sephton et al., 2000). As mentioned earlier, the CAR is a separate phenomenon from cortisol's diurnal rhythm (Fries et al., 2009), and consistent with the notion that the CAR may distinctively signify health consequences (e.g., the CAR, Kudielka and Kirschbaum, 2003), it cannot be discounted as a valuable biomarker of HPA axis activity.

Dmitrieva et al. (2013), studying adults ranging in age from 34 to 87, determined that men and women's diurnal cortisol data best fit three distinct profiles: a normative diurnal curve, distinguished by a robust CAR and diurnal slope, and lower awakening and bedtime levels (displayed by 73% of participants); an elevated curve, as indicated by higher morning values, coupled with a minimal CAR, and higher bedtime values (20% of participants); and a flattened curve characterized by a lower CAR, lower slope, and higher evening cortisol levels (7% of participants). Older age was associated with a greater probability of fitting an elevated diurnal curve (i.e., higher cortisol across the entire day), including waking levels that were 50% higher than those observed in the normative curve. The odds of experiencing an elevated cortisol day increased 2% with each year of age. The authors speculated that the elevated profile could signify GC hypersecretion, a scenario in which repeated exposure to stress produces chronically elevated levels of GCs, which could help predispose individuals to health decrements associated with aging (Dmitrieva et al., 2013). In addition, participants who were older and male tended to show a flattened cortisol profile. A one-year increase in age was correlated with a 2% greater likelihood of exhibiting a flattened curve for both sexes. When the sample was analyzed separately by sex, the probability of having a flattened profile decreased by 42% among women compared to men. Overall, it is plausible that subtypes of diurnal cortisol patterns develop according to both age and sex.

In a separate study, Adam et al. (2006) assessed older adult men and women to examine associations between prior-day and same-day demographic and cortisol variables. Similar to Dmitrieva et al.'s (2013) findings, Adam and colleagues found that participants who were older and male had marginally flatter diurnal cortisol slopes resulting either from a lower waking value or higher evening levels. In contrast with the Dmitrieva et al. (2013) findings, however, the Adam et al. (2006) results were at a trend level ($p < 0.08$). These tenuous results may have been obtained because the latter study used a more restricted age range (50–68) compared to the Dmitrieva et al. (2013) study, as well as examining a significantly smaller sample (156 vs. 1101).

Among these reports, a recent investigation conducted by Nater et al. (2013) is singular due to its high number of daily cortisol assessments (i.e., seven daily time-points across 10 days), exclusion criteria (e.g., thyroid dysfunction, psychological disorders, substance abuse, and dementias), and control of variables known to affect cortisol sampling (e.g., sex, smoking; see Table 1). Older age was positively associated with greater diurnal cortisol output (i.e., AUCg) over the course of the day. Older adults also exhibited a greater CAR and flatter wake-to-evening slopes compared to middle-aged and young adults. Nater et al. (2013) hypothesized that age-associated increases in endocrine functioning might represent a collective signature of lifetime stress. The authors also recommended that future work examine whether similar changes in diurnal cortisol are observable in older adults not screened for adverse health conditions, compared with the older adults who were screened in this study.

2.1.3. Conclusions from diurnal cortisol research—Several patterns emerged from the reviewed studies of older adults. First, the broader pattern of cortisol's diurnal rhythm (i.e., higher cortisol in the early morning and lower cortisol in the evening) appears to be preserved during aging (Van Cauter et al., 1996; Van Coevorden et al., 1991). Second, cortisol output seems to increase with age (Karlamangla et al., 2013; Nater et al., 2013), potentially beginning with the CAR (Almeida et al., 2009b). If the mechanisms influencing the CAR are more sensitive to alteration/dysregulation, and alteration occurs gradually as people age, then age differences in the CAR may be observed before changes in other aspects of the diurnal rhythm. Some researchers also reported that age correlates with a flatter diurnal slope (Adam et al., 2006; Dmitrieva et al., 2013; Karlamangla et al., 2013; Nater et al., 2013), which could be attributed to either lower morning cortisol and/or higher evening cortisol. Thus, existing evidence suggests that diurnal cortisol increases with age. However, as all studies reviewed were cross-sectional, additional longitudinal evidence is needed to solidify any claims of change with aging (vs. possible cohort effects). Also, it is unclear whether part or the entire diurnal rhythm is elevated in older adults, as either of these possibilities could contribute to higher cortisol.

Further, age-related changes in cortisol appear to be more distinct for men (Adam et al., 2006; Karlamangla et al., 2013). Compared to women, men exhibited a flatter slope with greater age (Adam et al., 2006; Dmitrieva et al., 2013), as well as a greater CAR (Almeida et al., 2009b), peak, nadir and overall output (i.e., AUCg; Karlamangla et al., 2013). Men's higher age-induced cortisol levels could reflect greater cumulative stress or may arise from metabolic differences observed earlier in the lifespan. For example, men generally show a

greater cortisol response to acute stress (Kudielka and Kirschbaum, 2005). If aging does increase men's cortisol responsiveness and prolongs physiological recovery after daily (i.e., acute) stress or challenge (Van Cauter et al., 1996), then this phenomenon could alter men's HPA regulation and lead to broader sex-specific changes in diurnal cortisol levels. Subtypes of age-related patterns of cortisol (Dmitrieva et al., 2013; Kumari et al., 2010a,b; Lupien et al., 1994, 1996; Sharma et al., 1989) might also produce differing results. As observed by Dmitrieva et al. (2013), within a sample there may be unequal groups of individuals with diurnal cortisol subtypes. If a study included a higher proportion of individuals expressing one subtype (e.g., elevated) over another (e.g., flattened), then the study's overall results could show higher morning versus evening cortisol within a pattern of greater output. The possibility of cortisol subtypes in older adults represents an intriguing area for future research.

Another area for future work is to determine whether the observed age-cohort differences in cortisol are associated with (1) aging itself, (2) exposure to stress, or (3) poor health/disease. As mentioned earlier, it is important to distinguish between older adults who are very healthy (and may not be representative of the greater population) and those who are relatively healthy (and more representative of normal aging). In contrast with other studies, Nater et al. (2013) evaluated cortisol in a greater number of samples per day and over a longer period of time (i.e., 10 days) and, therefore, reported the strongest evidence yet for cross-sectional differences in cortisol. Still, it is possible that the Nater et al. (2013) findings are not generalizable to the adult population due to their strict exclusion criteria.

In less healthy samples, adverse health conditions have been associated with an altered CAR or flatter slope (e.g., Hackett et al., 2014; Hek et al., 2013; Kumari et al., 2009, 2010a,b; Nater et al., 2008; Sephton et al., 2000), which may be a signature of hypo- or hypercortisolism (Miller et al., 2007). For example, Dmitrieva et al. (2013) found that adults with poorer health were more likely to exhibit a flattened diurnal slope. Other studies (e.g., Dmitrieva et al., 2013; Karlamangla et al., 2013) examined less healthy (and thus likely more generalizable) samples, with potential greater variability in cortisol levels. Those samples may have been more representative of the American aging population, who commonly suffer from various adverse health conditions (AARP Public Policy Institute, 2009). Greater variability in health status could have obscured the increased cortisol that was observed in healthier adults (i.e., those with few, or at least fewer, adverse health conditions).

Nater et al. (2013) also statistically controlled for sex, and therefore, did not report differences between men and women's cortisol. Sex differences may emerge only when comparing the sexes directly in analyses, as in other studies (Adam et al., 2006; Dmitrieva et al., 2013). Finally, as mentioned before, all of the studies reviewed above were cross-sectional, which limits our ability to understand how HPA axis functioning changes over the course of aging. Longitudinal, within-subject studies that examine HPA activity across adulthood will offer the opportunity to target when and where changes in cortisol occur, as well as demographic differences in diurnal cortisol output.

If future longitudinal research does confirm that diurnal cortisol does in fact increase and/or that the diurnal rhythm flattens with age, then the next step would be to determine whether

those changes are due to age-related alterations in GC, GR, or other neuroendocrine mechanisms. One possible mechanism for changes in cortisol level or pattern is changes to GC sensitivity, which is plastic throughout the lifespan and is affected by acute stress, exercise, and psychopharmacological treatment (Pariante et al., 2004; Rohleder et al., 2003). A variety of mechanisms may lower GC sensitivity (Pariante, 2006; Sapolsky and Plotsky, 1990). One possibility is that older adults may display age-related changes in GC sensitivity —for example, fewer GR overall, and/or GR in the brain or in peripheral tissues becoming less sensitive to GCs (Ferrari et al., 1995)—which would impair negative feedback and thereby cause increased cortisol (Sapolsky et al., 1986). Alternatively, Chahal and Drake (2007) proposed that there are age-related differences in the neuroendocrine mechanisms coordinating 24-h HPA axis release of GCs. Those alterations could lead to increased and inconsistent diurnal cortisol levels, such as the greater cortisol variability observed by Karlamangla et al. (2013). Either of these scenarios could be produced either by cumulative effects of lifetime stress, and/or by the normal aging process. Aging in both very healthy older adults and in the normative older adult population (i.e., in which some have adverse health conditions) may entail any combination of these mechanisms, producing impaired HPA axis negative feedback and higher cortisol output.

Even if there are observable physiological differences in older adults' HPA axis activity, we must ask whether those patterns actually reflect dysregulation and are truly detrimental to health. It is at least reasonable to propose that altered HPA axis functioning could predispose healthy older adults to health consequences. For example, chronically elevated cortisol is associated with both poor immune-system functioning (Lovallo and Thomas, 2000) and memory impairment via effects on the hippocampus (Wingenfield and Wolf, 2014). Altered GC sensitivity could be one mechanism behind elevated cortisol and/or health effects that have been associated with elevated cortisol. Importantly, there may be an optimal range for GC sensitivity: *reduced* GC sensitivity has been documented in some clinical groups (e.g., those with depression; Abercrombie, 2009; Holsboer, 2001), whereas individuals with other conditions (e.g., high blood pressure or PTSD; Walker et al., 1998; Yehuda, 2006) exhibit *increased* GC sensitivity above controls (see also Rohleder et al., 2010). A study that unintentionally included adults with health conditions that exert opposing effects on GC sensitivity (e.g., depression and high blood pressure) which, in turn, might subsequently increase or decrease diurnal cortisol, could find null results overall. If healthy aging actually does increase diurnal cortisol, then it will be important to distinguish direct age-related changes from indirect alterations caused by other endocrine conditions, physiological effects, or pathophysiological states (Chahal and Drake, 2007).

The reviewed research examined the process of diurnal cortisol secretion while people led typical lives. As mentioned earlier, it is well established that cortisol increases in response to an acute challenge or threat (Dickerson and Kemeny, 2004). The HPA axis may also become dysregulated due to chronic stress (Miller et al., 2007). Thus, researchers have speculated about age-related changes in *acute* stress-induced cortisol (as opposed to potential age-related changes in basal/diurnal cortisol, as reviewed above). Effects on stress-induced cortisol have been reviewed elsewhere, with authors reaching different conclusions: age may increase cortisol secretion in response to stress, particularly in women (see Otte et al., 2005, for a meta-analysis), versus age does not affect cortisol reactivity to stress (see Lai, 2014, for

a review). Of the two reports, Otte et al. (2005) included more studies (45 vs. 7) and was a quantitative meta-analysis (vs. Lai's qualitative meta-analysis), which increases our confidence in Otte et al.'s conclusion that stress-induced cortisol may increase with age. It is possible that older adults' normative higher diurnal cortisol stems from the same root cause(s) as the exaggerated cortisol response to stress in older adults. That is, decreased GC sensitivity with age could impair negative feedback that, in turn, could produce higher stress-induced peaks in cortisol and prolong the stress response (Sapolsky, 2005). In other words, dysfunctional negative feedback resulting from lower GC sensitivity could drive both normative higher diurnal cortisol and higher cortisol responses to acute stress in older adults. Given the differences between study results, additional research is needed to address this question by comparing both stress-induced and diurnal cortisol in very healthy versus typically aging (i.e., somewhat less healthy) older adults.

3. Psychosocial factors of resilience in older adults

Despite potential greater vulnerability to HPA axis dysregulation, many older adults exhibit extraordinary resilience (Hildon et al., 2008). Emotion regulation and the social environment have emerged as two of many predictors of resilience (Fredrickson et al., 2003; Ong et al., 2009; Tugade et al., 2004). In younger adults, these resources appear to be protective against maladaptive HPA axis responses (see DeVries et al., 2003, for a review), and may be exceptionally meaningful for older individuals with more limited resilience resources (Ong and Bergeman, 2004) or altered physiological fitness (e.g., higher diurnal cortisol; Nater et al., 2013). Emotion regulation and social support appear to influence older adults' HPA axis functioning, including cortisol (Cacioppo and Hawkley, 2003; DeVries et al., 2003; Kiecolt-Glaser et al., 2002), and may be predictive of their well-being (Charles and Carstensen, 2009).

Older adults also use emotion regulation and social networks differently, especially when navigating stressors that are uniquely associated with aging (e.g., cognitive and physical decline; Bonanno et al., 2004; Resnick, 2008). In the next section, we review connections between emotion regulation, social support, and diurnal cortisol to hypothesize how older adults' resilience affects the HPA axis. As we did with the diurnal-cortisol research discussed earlier, we selected studies to review in which the investigators assessed cortisol at least three times per day across three or more days[3] to produce trait-like diurnal cortisol levels (see Table 2 for study details). Conclusions provide support for the model of aging, stress and resilience introduced in the final section.

3.1. Emotion regulation and resilience

Emotion regulation refers to "the process by which individuals influence which emotions they have, when they have them, and how they experience and express these emotions" in a given situation (Gross, 1998, p. 275). Emotions and emotional regulation may be particularly central to resilience in later years, which are characterized by certain changes in emotional processes (Kessler and Staudinger, 2009; Ong et al., 2009). Specifically, adults'

[3]The one exception to the inclusion criteria was a study by Lai et al. (2012), in which eight samples per day were collected across two days, providing a high density of cortisol samples that was similar to the samples in the other reviewed studies.

ability to appraise and regulate emotional responses typically increases with age (Charles and Piazza, 2009; Labouvie-Vief et al., 1989). Further, negative affect levels decrease beginning in early adulthood through middle age (Carstensen et al., 2000; Charles et al., 2001; Roberts and Mroczek, 2008), and older adults appear to be better at predicting and controlling emotional arousal compared to younger adults (Nielsen et al., 2008). Older adults also display equivalent or better emotional control, which includes control of both which emotions are experienced and when emotion is expressed (Carstensen et al., 2000; Gross et al., 1997), as well as more effectively moderating both negative and positive emotion (Lawton et al., 1992). They also tend to report fewer negative reactions, and reappraise situations more positively compared to younger adults (Birditt and Fingerman, 2005; Birditt et al., 1995; Charles and Carstensen, 2007; Folkman et al., 1987; Tsai et al., 2000). Importantly, positive affect and negative affect are orthogonal dimensions that can change independently (Watson et al., 1988). Thus, age-associated changes in negative affect levels and regulation do not necessarily signify that older adults experience reciprocal changes in positive affect. Instead, age-related changes in emotion regulation abilities may help individuals recover from stress-induced negative affect more rapidly.

Older adults who are more flexible and adaptive when managing their emotions (e.g., Ong et al., 2009; Orgeta, 2009) may show greater resilience, particularly in response to different types of stressors, compared with either less resilient peers or younger adults. Adults with greater emotion regulation abilities exhibit greater resilience to the detrimental effects of stress and recover more quickly after stress (Ong et al., 2006). Older individuals use emotional regulation skills to manage emotional (and stressful) situations differently from younger adults (Birditt and Fingerman, 2005; Blanchard-Fields et al., 1995; Scheibe and Blanchard-Fields, 2009; Watson and Blanchard-Fields, 1998). When stressors are emotional and interpersonal (e.g., conflict with friends or family), older adults endorse more passive, emotion-focused strategies (e.g., not directly handling the issue; Blanchard-Fields et al., 1995; Blanchard-Fields et al., 1997). Although these coping strategies may be unhealthy for younger adults, they appear to benefit older adults (Gross, 2002). Older adults are also confident about their emotion regulation skills, rating themselves highly on self-reported emotion regulation abilities (Gross et al., 1997; Lawton et al., 1992; Phillips et al., 2006). Emotional self-efficacy could underlie age differences in affective experience (Carstensen et al., 2003; Kessler and Staudinger, 2009; Shiota and Levenson, 2009). Thus, appropriate emotional expression (e.g., higher positive affect) may be reinforced by efficient emotion regulation. If older age is associated with increases in subjective well-being (Cacioppo et al., 2008), then greater self-knowledge of emotion regulation processes may underlie the benefits of those emotional strategies for health and resilience.

3.1.1. Emotion regulation and diurnal cortisol—Do older adults' patterns of emotion and emotion regulation relate to their HPA activity? In one study, healthy older adults viewed negative/arousing and neutral/non-arousing pictures while blood oxygenation, an indicator of neural activity, was assessed with fMRI (Urry et al., 2006). While viewing each picture, participants engaged in an emotion regulation task in which they were cued to increase, decrease, or maintain negative affect. Participants provided diurnal cortisol samples during the week immediately following the fMRI session. Those who were more proficient

in decreasing negative affect concurrently displayed higher activity in the ventromedial prefrontal cortex (vmPFC), a structure implicated in emotion regulation, and reduced activation in the amygdala, a structure implicated in emotional response, as well as a steeper diurnal cortisol slope in the following week. The findings suggest that greater *voluntary* emotional control may correlate with more optimal diurnal cortisol secretion. There are several possibilities that could help to explain this correlation. First, perhaps having better emotion regulation abilities contributes to better regulation of cortisol. Alternately, improved HPA axis control may improve individuals' emotion regulation abilities. And finally, a third variable (e.g., vmPFC functioning) may influence both HPA axis and emotion regulation. Although the direction of these effects are uncertain, the Urry et al. (2006) findings offer preliminary evidence associating older adults' adaptive emotion regulation abilities with diurnal cortisol.

Several other studies report an association between older adults' cortisol levels and emotion. In middle-aged and older adults, greater negative affect (e.g., loneliness, sadness, and feeling threatened) on one day was associated with an increased CAR on the following day, suggesting that short-term negative emotion may be coupled with next-day physiological effects (Adam et al., 2006). Higher negative emotion experienced during one day was also associated with higher same-day evening cortisol levels. To explain these results, Adam et al. (2006) proposed the "boost" hypothesis in which the CAR may be an adaptive response to stressful experiences the previous day, which provides a person with a physiological "boost" (i.e., an increased CAR) in order to address the demands of the following day. Thus, these researchers hypothesized that the experience of negative affect or poorer regulation of negative emotion may produce temporary alterations in daily cortisol patterns. Over time, these patterns of negative emotion and their effects on diurnal cortisol may become consistent, as in the case of chronic stress, to generate broad, systematic changes in physiological health (e.g., hypercortisolism).

In another investigation, Wrosch et al. (2008) evaluated whether baseline trait affect and diurnal cortisol would predict older adults' physical symptoms. Basal diurnal cortisol was unrelated to initial health. However, in a three-way interaction, greater basal diurnal cortisol, higher negative affect, and poor sleep predicted worse health two years later. These findings suggest that increased diurnal cortisol may predict long-term poor health, but only for adults who also report high negative affect and inefficient sleep. As Wrosch et al. (2008) did not find a correlation between affect and cortisol at baseline, it is possible that emotion-cortisol associations become more entrained over time (Adam et al., 2006) to affect long-term health adversely. Importantly, this study also demonstrated how other variables (e.g., sleep quality) could influence the interactions between cortisol, emotion, and emotion regulation.

Unlike the previous studies discussed, which only included older individuals, Piazza et al. (2013) examined age-cohort differences in cortisol and emotion in an NSDE sample of young and older adults. Higher daily negative affect was associated with greater diurnal cortisol, but only in participants who were 53 and older (the age range was chosen based on participants' grouping). Piazza et al. (2013) theorized that, although some research has found negative affect and cortisol to be associated at all ages, an adult's capacity to manage their physiological response to negative emotional experiences may decrease with age.

Possibly younger individuals are better at managing their physiological responses to negative affect. Consequently, earlier in adulthood, the relation between affect and cortisol may be "masked" by better physiological management, but become detectable later, as older individuals may have diminished abilities to manage their physiological responses. This idea aligns with the possibility that GC sensitivity and HPA axis negative feedback may become compromised with age (Sapolsky et al., 1986). Still, ample evidence shows that emotion regulation abilities improve during aging (e.g., Charles and Piazza, 2009; John and Gross, 2004; Labouvie-Vief et al., 1989; Phillips et al., 2008). Thus, an alternative possible explanation is that negative affect and diurnal cortisol are not linked earlier in life, but that the HPA axis becomes more attuned or responsive to negative-emotional experiences with age. If that explanation is correct, it could explain why negative affect and diurnal cortisol were correlated only in middle-aged and older adult participants, and not in younger adults, at least in the Piazza et al. (2013) study. Alternate patterns of findings have also been reported, as will be mentioned below.

Based on studies in younger adults, we can speculate about the connection (if any) between older individuals' emotion and HPA axis activity, at least in the context of acute stress. In a meta-analysis, Campbell and Ehlert (2012) examined younger adults' emotional and cortisol responses to an acute laboratory stressor involving social evaluation. Only 25% of the studies showed a significant correlation between cortisol and negative affect in response to stress, and there was no association between cortisol and positive affect. These results suggest that HPA axis activity (i.e., cortisol) is a separate construct from emotional (particularly negative affect) responses to stress, not a marker of those, and that the two constructs are dissociated in younger cohorts. If the constructs are similarly dissociated later in life, then older adults could show briefer or less negative emotion, but more or prolonged stress-induced HPA activation. Alternately, the effects of stress on resultant affect and HPA axis activity may become entrained with age (Adam et al., 2006).

Emotion regulation may become more challenging for older adults who are faced with chronic stress. In an investigation of older adults who did and did not experience chronic stress (specifically, spousal bereavement), higher trait negative affect predicted lower levels of waking cortisol—in other words, a less typical diurnal pattern—in adults who were bereaved (Ong et al., 2011). Interestingly, there was no affect-diurnal cortisol association in non-bereaved adults, paralleling results observed in other non-stressed older adults (e.g., Ice, 2005). A second finding was that lower trait positive affect mediated the impact of stress (i.e., bereavement) on the diurnal cortisol slope (Ong et al., 2011), whereas lower positive emotion in bereaved individuals' was associated with a flatter slope. As positive affect and negative affect correlated with different cortisol measures, these findings add to the already considerable evidence that these two broad dimensions of emotion do not change reciprocally (Watson et al., 1988). Overall, the Ong et al., (2011) results suggest that emotion may affect the HPA axis differently during chronic stress compared to no chronic stress. Notably, the group without bereavement may still have been managing other kinds of chronic stress, which complicates interpretation of the findings.

3.1.2. Conclusions about emotion regulation and diurnal cortisol—Research suggests that during basal (i.e., unstressed) conditions, older adults' emotions/affect

correlate with measures of diurnal cortisol (e.g., Adam et al., 2006; Piazza et al., 2013) as well as with the associations between cortisol and health (Wrosch et al., 2008). van Niekerk et al. (2001) reasoned that older adults' cortisol may react selectively to negative affect and not to positive affect. Parallel findings exist from younger adults as well, i.e. no relationships between positive affect and cortisol (Campbell and Ehlert, 2012). If true, this hypothesis would help to explain why some studies have found an association between basal diurnal cortisol and negative affect (Adam et al., 2006; Ice, 2005; Wrosch et al., 2008). In contrast, only one study has reported evidence linking high arousal positive affect with diurnal cortisol (i.e., a steeper slope and lower evening cortisol; Hoyt et al., 2015); however, this investigation was conducted in a young adult and youth sample, so further research is needed to determine whether the finding generalizes to older adults. Thus, associations between older adults' negative and positive affective and endocrine states may not be reciprocal (e.g., high negative affect with high cortisol and high positive affect with low cortisol). The observed associations between diurnal cortisol and emotion may also change when older adults are challenged by acute or chronic stress (e.g., Ong et al., 2009).

As observed by Adam et al. (2006), there is preliminary evidence of within- and between-day psychobiological pathways connecting cortisol with emotion. Older adults' transient daily emotional experiences and cortisol alterations may become coupled over time, resulting in long-term effects on the HPA axis and other health consequences (Adam et al., 2006; Piazza et al., 2013). Additional work using multi-day designs is required to capture longitudinal changes in the emotion regulation–HPA axis association. This research could reveal more nuanced affect-cortisol interactions and disentangle the exchange between age-related signatures of emotion regulation and HPA axis activity.

3.2. Social support and resilience

Resilience researchers have also emphasized the importance of social support for resilience (Ong et al., 2009; Ryff and Singer, 2000). Social support is a fundamental resource for managing stress across the lifespan, and social networks especially facilitate quality of life and well-being during later years (Antonucci and Akiyama, 1991). *Social support* is defined as various types of assistance or help that people receive from others (Seeman, 2008) and has been divided into two main types. Instrumental support consists of information or tangible acts (e.g., assisting with finances or transportation) provided by others. Emotional support consists of others' actions that are intended to "make us feel loved and cared for that bolster our sense of self-worth (e.g., providing encouragement or positive feedback)" (Seeman, 2008). For older adults, emotional support appears to be more beneficial than instrumental support. Older adults who report receiving moderate or high emotional support have a lower mortality risk (Penninx et al., 1997) and display better emotional well-being (Bisconti et al., 2006) than those who receive low emotional support. High levels of instrumental support are tied to *increased* mortality (Penninx et al., 1997) and poorer health (Bisconti et al., 2006), most likely due to the greater need for instrumental support when managing later life health conditions.

Older adults' characteristic patterns of social support include preferring familiar social partners (Carstensen et al., 2003; Fredrickson and Carstensen, 1990) and maintaining

smaller, but closer, social ties compared to younger adults (Lang, 2001). Changes in expectations of affiliation may increase older individuals' satisfaction with social relationships despite the decreasing size of their support networks (Shaw et al., 2007). Cross-sectional investigations of adults' social interactions and receipt of social support reveal that older men may have more limited social support compared to women. Older men endorsed having smaller social networks and/or less social contact (Almeida et al., 2009b; Depner and Ingersoll-Dayton, 1988; Krause and Borawski-Clark, 1995; Lang and Carstensen, 1994; Murrell and Norris, 1991), lower emotional support (Antonucci and Akiyama, 1987; Depner and Ingersoll-Dayton, 1988; Turner and Marino, 1994), and greater dependence on their partner (Antonucci and Akiyama, 1987). Overall, in contrast to older women, older men likely have lower social resources to promote resilience and to aid stress management.

Some evidence suggests that higher levels of social connectivity may protect against mental and physical illness in older adults (e.g., Southwick et al., 2005; Uchino, 2004). Conversely, loneliness and social isolation have been found to be prominent markers of lower social resources and to predict poor psychophysiological health (see Hawkley and Cacioppo, 2010 for a review). Netuveli et al. (2008) identified adults aged 50 years or older who had experienced the onset of a major chronic stressor (i.e., bereavement or marital separation, poverty, or functional limitation) within the past year. The stressor's impact was measured using repeated annual assessments of the General Health Questionnaire 12 (GHQ-12, a measure of psychiatric symptoms; Golderberg and Williams, 1988) and the researchers operationalized resilience as reporting an increased GHQ-12 score following the stressor's onset yet returning to the individuals' pre-stressor onset score at the next annual assessment. The authors used a median split of participants' self-reported social support to create high and low support categories at each measurement point (pre-onset, shortly post-onset, and 1-year follow-up). Resilient adults were more likely to have high social support at all three time points than non-resilient adults. High pre-stress support increased the likelihood of being resilient by 40–60% compared to those with low pre-stress support. These findings emphasize the value of social support in promoting resilience and well-being when recovering from a major stressful event. The longitudinal methodology also highlights how social support contributes to the process of resilience. Viewing resilience as a process (vs. a static trait) is particularly important for older adults (Montpetit et al., 2010), whose social networks contribute to resilience, but are likely to decrease over time.

3.2.1. Social support and diurnal cortisol—HPA axis activity is one candidate mechanism that may interact with social support to affect health outcomes (Kirschbaum et al., 1995; Thorsteinsson and James, 1999). Few studies have investigated such relationships in older adults, but their findings have provided some insight into pathways between diurnal cortisol and social support. In one investigation, Friedman et al. (2012) characterized connections between social strain and cortisol in adults. Self-reported social strain (i.e., social-network stress or interpersonal exchanges that induced psychological stress) with family and friends was assessed both 10 years prior to, and concurrent with, the measurement of diurnal cortisol. The two waves of self-report data were combined to create composite strain scores. Older adults (aged 65 and older) who experienced greater social

strain exhibited increased evening cortisol and a flatter cortisol slope. The association was not found for younger adults (less than 50 years old). This study provides some evidence that older adults' HPA axis may be more sensitive to the effects of chronic social stress, and the way in which lower social support (and lower resilience) is associated with biological vulnerability.

Researchers have also examined associations between older adults' social support and the CAR. As mentioned earlier, Adam et al. (2006) found that greater loneliness reported on one evening predicted a higher next-day CAR. This finding suggests that there may be a time lag between experiencing factors that contribute to—or, conversely, detract from—resilience (i.e., higher support/lower social strain vs. isolation or higher strain) and subsequent, short-term changes in cortisol. In another study, Lai et al. (2012) measured older men's diurnal cortisol and social-network characteristics, including social-network cultivation, size, and emotional support. Men who devoted more effort to developing and strengthening their social relationships (i.e., cultivation) exhibited a greater CAR and a steeper diurnal decline, typical features of diurnal cortisol patterns often associated with health. Social-network size and emotional support were unrelated to diurnal cortisol. Cultivation likely represents positive motivation to actively seek affiliation and sustain social support. The findings provide some support for the idea that maintaining quality social relationships may offer protection against altered HPA functioning and stress in older age.

The Lai et al. (2012) and Adam et al. (2006) findings dovetail, despite initially appearing contradictory. Adam et al. (2006) suggested that the higher CAR following a day of loneliness could actually mobilize energy for a more socially engaged day than on the previous one and could work to restore more adaptive functioning. Thus, higher CAR may be associated with social network cultivation in both studies. Also, a greater CAR and a steeper diurnal decline (from a trait perspective) are normative diurnal characteristics of HPA activity that have been associated with healthier states, and may not signify the same thing as a single elevated CAR after a day of loneliness (CAR from a state perspective). Although Adam et al. (2006) examined day-to-day state changes in cortisol and loneliness, whereas Lai et al. (2012) assessed trait cortisol and social-network characteristics, the higher next day CAR identified by Adam et al. (2006) may signify the same broader cultivation process identified by Lai et al. (2012).

Social resources may truly benefit health when combined with advantageous emotion regulation. Rueggeberg et al. (2012) examined data from the Montreal Health and Aging Study to determine whether using self-protective positive reappraisal and external attributions (e.g., avoiding self-blame) when faced with a health problem would prevent higher diurnal cortisol in lonely older adults. Cortisol AUCg over the course of a day was assessed at baseline and 2 years later. Baseline self-protection predicted decreased cortisol among lonely participants, but not for those who did not report loneliness. Thus, self-protection may have helped to reduce diurnal cortisol in lonely adults. Perhaps self-protection can substitute for missing social support. Looked at another way, older adults who are not lonely may rely less on health-related self-protection to buffer against stress (Rueggeberg et al., 2012).

3.2.2. Conclusions about social support and diurnal cortisol—Social networks are a vital resource for resilience. Older adults display specialized patterns of social-support utilization, with smaller social circles but more valued social connectivity (Lang, 2001; Shaw et al., 2007). There are also many proposed connections between social networks and health (see Uchino, 2006, for a review). For example, greater social support has been associated with improved cognition in older age (e.g., Seeman et al., 2001; Sims et al., 2014) and better quality of life while managing chronic pain (e.g., Jakobsson and Hallberg, 2002). Alternately, social networks can produce negative effects such as those resulting from social strain (Friedman et al., 2012) or the chronic stress of caregiving (e.g., Monin and Schulz, 2009). Older adults who thrive seem to construct social networks to optimize the receipt of instrumental and emotional support in anticipation of managing daily challenges as well as chronic stressors. As summarized by Ong et al. (2009), “the soothing power of social connection depends on our ability to select engagements that both preserve emotional well-being and bolster coping efficacy” (p. 1784).

One way that social support may contribute to later life resilience is by interacting with HPA axis activity. Some evidence shows that a higher quality of social support and utilization is correlated with lower cortisol overall and/or a more robust daily slope (Adam et al., 2006; Lai et al., 2012; Rueggeberg et al., 2012). If this is the case, merely increasing the frequency of social contact may be insufficient for affecting HPA axis activity (Uchino et al., 1996). The association between older adults’ diurnal cortisol and social support could also be moderated by individual differences in coping mechanisms, such as motivation to improve social networks (i.e., cultivation; Lai et al., 2012). Given that older men and women demonstrate different patterns of social support (e.g., Almeida et al., 2009b), sex differences in support may also moderate associations between HPA functioning, health and longevity. Finally, social support and HPA axis activity may interact differently in a chronically stressed versus an unstressed sample. Overall, it is apparent that social support contributes to resilience across the lifespan, potentially in part by affecting HPA axis activity. Even as social networks transform during aging, social support remains a vital resilience resource later in life.

4. Integrating age-related diurnal cortisol with resilience

In this review, we have drawn attention to diurnal cortisol as a key HPA axis biomarker that is shaped by psychosocial experience and that is crucial for understanding resilience and health in aging. We primarily reviewed studies that included multiple cortisol samples collected over many days in order to examine stable cortisol variables; such an approach speaks more to chronic than to acute stress. To summarize our primary conclusions: (1) The best available evidence suggests that aging is correlated with increased diurnal cortisol levels and flattened cortisol slopes (e.g., Nater et al., 2013), although this conclusion is based on cross-sectional research only. Some, but more limited research indicates that (2) higher negative affect and social isolation are also associated with significantly elevated diurnal cortisol, whereas (3) older individuals who use flexible emotion regulation and maintain quality social relationships exhibit lower cortisol levels. Thus, we hypothesize that emotion and social constructs influence resilience by modulating HPA axis perturbations related to aging and/or cumulative effects of stress.

In addition to their distinct benefits, the psychosocial processes that contribute to resilience appear to be highly integrated. For example, adults who reported lower levels of social connectivity also had greater difficulty modulating negative emotion after stress (Ong and Allaire, 2005). Greater social support may in fact promote more positive emotions in older adults, as well in younger age groups (Carstensen et al., 2003). This research is consistent with Socioemotional Selectivity Theory (SST; Carstensen et al., 2003; Löckenhoff and Carstensen, 2014). Carstensen et al. (2003) hypothesized that there is an adaptive narrowing of later life social networks, in addition to prioritizing emotion-focused over problem-focused coping (Carstensen et al., 2003; Löckenhoff and Carstensen, 2014). Baltes and Baltes' (1990) Theory of Selection, Optimization, and Compensation echoes the SST. These researchers theorized that some older individuals (i.e., those who are more resilient) maximize the gains and minimize the losses that are hallmarks of aging more than individuals who are less resilient. In light of the reviewed literature, when faced with acute or chronic stress, those older adults may *compensate* for the physiological deficits that accompany aging (such as potential HPA dysregulation or simply higher diurnal cortisol) by *optimizing* their emotion regulation skills and available social relationships. Selection, optimization, and compensation could still occur without higher trait diurnal cortisol, but may become even more meaningful for older adults with elevated cortisol. Thus, more resilient older adults could adapt to chronic stress by optimally using age-related changes in psychosocial resources and skills (Bonanno et al., 2004; Resnick, 2008).

4.1. A Model of Aging, Stress, Resilience

The proposed *Aging, Stress, and Resilience Model* (ASRM; see Fig. 1) summarizes the reviewed research by depicting multiple pathways between aging, chronic stress, HPA axis activity (i.e., diurnal cortisol), resilience, and health outcomes. In the model, one-directional lines signify causal associations that have relatively strong supporting evidence (e.g., emotion regulation abilities increase with age; Gross et al., 1997; Lawton et al., 1992; Phillips et al., 2006). Lines with double arrows indicate bidirectional associations between constructs (e.g., reciprocal effects between resilience and positive health outcomes), which are supported by correlational evidence. Each arrow is also tagged with a positive and/or negative sign, indicating whether the first construct initiates an increase and/or a decrease in the second construct (e.g., aging can increase and/or decrease aspects of social support). Notably, there are likely (1) other associations among the constructs in the model and, (2) associations between the described constructs and other constructs that are not depicted in the ASRM. However, for simplicity, we include only those constructs and relations that were the main focus of this review.

We next review the constructs in the model. *Aging* was a primary topic in this review, and is therefore a central focus of the ASRM. Of note, in this model we conceptualize aging as simply getting older (time passing), rather than the biological processes of aging. The effects of aging are moderated by a variety of individual and demographic variables, including sex differences (Antonucci and Akiyama, 1987; Kirschbaum et al., 1995; Kudielka and Kirschbaum, 2005), as highlighted throughout this review. We also examined *Chronic Stress*, the model's second construct. As stated earlier, chronic stress can involve prolonged or ongoing stress (Miller et al., 2007; Rosnick et al., 2007; Uchino et al., 2001); in addition,

over time and repeated events, frequent acute stress can engender chronic stress (Miller et al., 2007). In most of the reviewed studies, it is difficult to determine how acute stress and chronic stress are related. We generally restricted the reviewed studies to those that examined diurnal cortisol over at least three days in order to evaluate HPA axis activity primarily resulting from older adults' chronic (or longer-term; trait rather than state) stress. Aggregating at least three days of cortisol data begins to tap into trait-driven rather than state-driven cortisol levels, which helps to rule out effects due to a single acute stressor. Thus, trait-like cortisol, in part, reflects ongoing chronic stress.

Although we defined most constructs in the ASRM based on their respective literatures, we used an operational definition of HPA axis activity, according to older adults' patterns of diurnal cortisol reviewed above. Specifically, in line with our conclusions about cross-sectional differences in older adults' cortisol, the construct of *Diurnal Cortisol* includes an elevated CAR, a greater diurnal AUCg, and a flatter morning-to-evening cortisol slope (Adam et al., 2006; Almeida et al., 2009b; Dmitrieva et al., 2013; Karlamangla et al., 2013; Nater et al., 2013). Of course, there are other ways to conceptualize HPA axis activity, because it includes both state (i.e., acute stress-induced) and trait (i.e., basal diurnal cortisol, chronic stress-related) components, but using a more specific operational definition permitted a more focal examination of the relevant literature.

Further reviewed evidence indicates that older adults' diurnal cortisol may be modulated by, and/or may interact with, psychosocial variables that promote resilience. *Emotion Regulation* is one psychosocial factor that contributes to *Psychological Resilience* (i.e., resilience). Emotion regulation includes discrete reports of positive or negative affect, but is more accurately defined as how well an individual manages positive and negative affect and uses techniques such as emotional-lability and affect optimization (Carstensen et al., 2000; Gross et al., 1997; Lawton et al., 1992). *Social Support* is a second psychosocial factor that contributes to resilience. Older adults' typically show a different pattern from younger adults in their needs for instrumental and emotional support, and often reduce the size of their social networks. Importantly, resilience is viewed in this model as a positive construct, but resilience resources are subject to change for older adults (Montpetit et al., 2010; Pearlin and Skaff, 1995). For example, losing a major source of social support (e.g., the death of a spouse; Bonanno et al., 2004; Ong et al., 2009) could decrease older adults' resilience. Finally, as this review also examined how resilience affects older adults' health and well-being, we chose to focus on *Positive Health Outcomes,* including physiological and psychological health. Aging, chronic stress, emotion regulation, social support and resilience all affect positive health outcomes.

To describe the depicted ASRM pathways briefly, the process of *Aging* first affects *Chronic Stress*. The term "aging" typically evokes negative associations of chronic stress (e.g., bereavement, health declines, and loss of functionality; Moss et al., 2001; Ong et al., 2006), yet other events that occur during aging may reduce chronic stress (e.g., retirement, relief from raising children). Therefore, as depicted in the model, aging can increase and/or decrease chronic stress. Increased chronic stress, in addition to the process of normal aging, could contribute to greater diurnal cortisol observed in older adults (e.g., Karlamangla et al., 2013; Nater et al., 2013). Alternatively, lower chronic stress in older adults' could slow the

possibility of altered diurnal cortisol or HPA dysregulation. Aging is also associated with improved emotion regulation abilities (e.g., Carstensen et al., 2000; Gross et al., 1997). However, aging can be accompanied by either an increase or decrease in emotional and instrumental support, and older adults' generally reduce the size of their social networks (Bisconti et al., 2006; Penninx et al., 1997). Finally, in general, aging decreases positive health outcomes.

Diurnal Cortisol contributes indirectly to positive health by interacting with emotion regulation and social support. *Psychological Resilience* modulates the association between age-related influences on diurnal cortisol and health. As explored in this review, *Emotion Regulation* and *Social Support* are two factors that contribute to psychological resilience (Ong et al., 2009; Fredrickson et al., 2003; Tugade et al., 2004). The link between emotion regulation and positive health outcomes is unidirectional: Older adults' improved emotion regulation abilities may contribute to their health (Gross, 2002; Ong et al., 2006). Similarly, older adults with high social support may be more resistant to adverse physical or psychological conditions (Southwick et al., 2005; Uchino, 2004), resulting in greater positive health outcomes. Although there appear to be associations between emotion regulation and diurnal cortisol (Carstensen et al., 2003; Ong and Allaire, 2005), as well as between social support and diurnal cortisol (Adam et al., 2006; Lai et al., 2012), more research is needed to determine the direction(s) of these associations in older adults. However, evidence does suggest that different aspects of social support may contribute to increases or decreases in diurnal cortisol (Adam et al., 2006; Lai et al., 2012; Rueggeberg et al., 2012). Aside from the effects of social support and emotion regulation—two aspects of resilience—on diurnal cortisol, little evidence exists regarding how resilience in general affects diurnal cortisol; this area warrants further investigation. Lastly, as noted with the bidirectional pathways, *Positive Health Outcomes* can both increase resilience and decrease the likelihood of experiencing additional chronic stress.

The ASRM is a preliminary theoretical model that highlights psychosocial and physiological factors that affect well-being in older age. The greater picture is no doubt significantly more complex than we have depicted but, for parsimony, we highlight only the reviewed constructs. In this review, we also have identified several opportunities to refine this model with additional research. First, although we have discussed age differences in these constructs, the ASRM's pathways are not all specific to older adults. Rather, several of the associations (e.g., effects of chronic stress on diurnal cortisol) represent typical relations observed across adulthood. More research is needed to determine age-related differences in the discussed associations.

Second, there are individual differences in each of the ASRM's constructs that complicate predicting endpoints and that need further explication through research. For example, many of the reviewed studies revealed sex differences (e.g., Adam et al., 2006; Dmitrieva et al., 2013) that may moderate the relationships described in the ASRM.

Third, diurnal cortisol is only one part of the larger HPA system, which in turn is only one part of stress-related neurobiology. Other aspects of the HPA axis and brain stress/emotion systems need to be researched and integrated into the ASRM. In other words, greater

knowledge of age-related variations in the HPA axis and other associated neurobiological factors in general is necessary to establish how psychosocial constructs affecting resilience interact with HPA activity.

Fourth, it will be crucial for future studies to include more frequent measurements of HPA axis activity (Nater et al., 2013) and resilience dimensions (Ong and Bergeman, 2004) across days, weeks, and years. This research will assist in examining whether age-cortisol associations differ in response to acute versus chronic stress, and to stress across different time frames. Some researchers have examined intraindividual changes in resilience factors (e.g., Ong et al., 2009); the ASRM's dual-direction feedback arrows are intended to help indicate this potential intra-individual change.

Fifth, in the reviewed studies, some researchers examined diurnal cortisol only across a given time frame, and others specifically examined cortisol in adults who were experiencing an acute stressor (e.g., bereavement). It will be crucial to assess both perceived and objective measures of stress to increase our understanding of how acute and/or chronic stress levels correlate with cortisol.

Overall, there is a clear need for longitudinal studies that incorporate detailed measurement of HPA axis activity and examine within-person changes in both resilience factors and biological variables across years. Such investigations will help to determine how age differences in cortisol develop over time. The cross-sectional studies examined in this review suggest age differences, but not necessarily changes in cortisol that are due to aging per se; in other words, the findings from all cross-sectional studies could reflect cohort differences. Therefore, researchers are limited in making inferences about changes with age without additional longitudinal work.

5. Conclusions

Aging is a complex process, and resilience is similarly multidimensional (Southwick et al., 2008). This review represents a preliminary effort to describe interactions between, on the one hand, a physiological biomarker of HPA axis activity (i.e., diurnal cortisol) and, on the other, psychosocial factors (i.e., emotion regulation and social support) that contribute to stress resilience. Limited but suggestive evidence indicates that older individuals have distinct patterns of diurnal cortisol, including greater diurnal cortisol output and a flatter diurnal slope (Adam et al., 2006; Almeida et al., 2009b; Dmitrieva et al., 2013; Karlamangla et al., 2013; Nater et al., 2013). The reviewed literature also raises the question of how to characterize "normal" cortisol in older adults. Older adults who are considered healthy for their age may still have compromised health when compared with younger adults. Therefore, it is difficult to make direct comparisons between older and younger cohorts' typical HPA functioning. If we define "normal cortisol" as the diurnal slopes observed in younger adults, and merely compare cortisol signatures between older and younger adults, then we may miss the complete picture of older adults' pathways between resilience, HPA axis activity, and health. If HPA dysregulation does occur as healthy people age, and/or due to health conditions that are common in older adults (AARP Public Policy Institute, 2009), then the process may not be avoidable or recoverable.

Greater resilience is associated with longevity and a better quality of life. On the other hand, if older adults experience unique chronic stressors, demonstrate age-related dysfunction in HPA axis activity, and also exhibit deficits in resilience, then the total risk could be exponentially more debilitating for health. Research on biological and psychosocial processes affecting resilience and well-being have largely proceeded independently, and connections between these two areas of research are not well established. Although there are likely multiple routes to resilience (Bonanno, 2004, 2005; Ong et al., 2006), based on the evidence presented in this review, we propose in the ASRM that emotion regulation and social support are two primary factors that contribute to resilience to chronic stress, potentially, in part, by modulating HPA activity in older adults. Our conclusions encourage further research examining age-associated changes in the emotional experience of, and biological consequences of stress. That knowledge will be important both to aid health professionals in discerning pathways to resilience and well-being into older age and to provoke new inquiries into psychological resilience across the lifespan.

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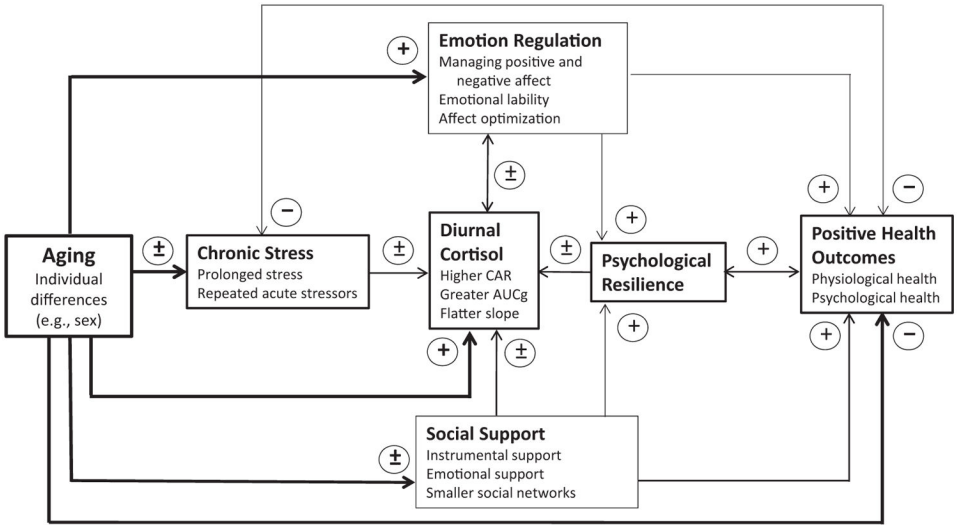

Fig. 1.

The Aging, Stress, and Resilience Model (ASRM). The ASRM depicts pathways between the constructs focused on in this review – aging, chronic stress, diurnal cortisol, psychological resilience, and health outcomes. See text for details.

Table 1

Sample characteristics and methodology from studies examining age effects on diurnal cortisol. All studies sampled cortisol at least three times per day over at least three days to better establish trait levels of diurnal cortisol.

Study	Participant Characteristics	Cortisol Sampling	Health Screen/Exclusions	Statistical Controls	Slope Calculation Method	Compliance Control
Adam et al. (2006)	*N* = 156 (48% women) Age range: 50–68 years M_{age} = 57, SD ± 4.5	Three daily samples on three days: • Awakening • 30 min post-awakening • Before bedtime	Self-reported health Exclusions: Use of steroid-based medication	Current psychiatric conditions, Tobacco use, Medication use, Time of awakening	Hierarchical linear modeling was used to fit diurnal cortisol slopes for each individual (cortisol levels are predicted by time since waking for each individual)	Electronic data collection monitoring used by 50% of the sample
Almeida et al. (2009a,b)	*N* = 1143 (55% women) Age range: 33–84 years M_{age} = 57, SD ± 12	Four daily samples on four days: • Awakening • 30 min post-awakening • Before lunch • Before bedtime	Screened for health conditions No specific exclusions reported	Sex, Smoking status, medication use, time of awakening	Multi-level growth modeling: Regressing CAR data against time of day	Smart boxes used by 25% of the sample
Dmitrieva et al. (2013)	*N* = 1101 (56.2% women) Age range: 34–87 years M_{age} = 58.2, SD ± 12.1	Four daily samples on four days: • Awakening • 30 min post-awakening • Before lunch • Before bedtime	Screened for health conditions Exclusions: abnormal cortisol samples No exclusions reported for health conditions	Age, Sex, Smoking status, Medication use, Global self-reported health, Adult stressful life experiences	Growth mixture modeling with latent time basis	Smart boxes used by 25% of the sample
Karlamangla et al. (2013)	N = 1693 (57% women) Age range: 25–74 years M_{age} and SD: unknown	Four daily samples on four days: • Awakening • 30 min post-awakening • Before lunch • Before bedtime	Screened for health conditions No specific exclusions reported	Smoking status, Depression, Time of awakening, BMI, Number of Major Chronic Health Conditions, Use of oral steroid medication, Use of depression or anxiety medication	Multi-level growth modeling	Smart boxes used by 25% of the sample
Nater et al. (2013)	*N* = 185 (51% women) Age range: 20–81 years M_{age} = 48.55, SD ± 19.19	Seven daily samples on ten days:	Self-reported health Exclusions: pregnancy, breastfeeding, thyroid	Sex, smoking status	Subtracting waking level from evening level	None

Study	Participant Characteristics	Cortisol Sampling	Health Screen/Exclusions	Statistical Controls	Slope Calculation Method	Compliance Control
		• Awakening • 30 min post-awakening • Every three hours until 9pm	dysfunction, mental disorders, substance abuse, dementias, endocrine conditions, BMI > 35, hormone-producing cancers, psychiatric medication, shift work			

Table 2

Sample characteristics and methodology from studies examining emotion, social support, and diurnal cortisol. All studies sampled cortisol at least three times per day over at least two days.

Study	Participant Characteristics	Cortisol Sampling	Health Screen/Exclusions	Statistical Controls	Slope Calculation Method	Compliance Control
Adam et al. (2006)	*N* = 156 (48% women) Age range: 50–68 years M_{age} = 57 years, SD ± 4.5	Three daily samples on three days: • Awakening • 30 min post-awakening • Before bedtime	Self-reported health and health behaviors; Exclusions: Steroid-based medication	Current psychiatric condition, Tobacco use, Medication use, Time of awakening	Hierarchical linear modeling is used to fit diurnal cortisol slopes for each individual (cortisol levels are predicted by time since waking for each individual)	MEMS Track Caps used by 50% of the sample
Friedman et al. (2012)	*N* = 1502 (55.93% women) Age range: 25–74 years M_{age} and SD: Not reported	Four daily samples on four consecutive days: • Awakening • 30 min post-awakening • Before lunch • Before bedtime	Self-reported health and health behaviors; No exclusions for health reported	Age, Sex	Piecewise linear growth curves and model-estimated mean slopes	Smart boxes used by 25% of the sample
Lai et al. (2012)	*N* = 78 (48.72% women) Age range: 59–86 years M_{age} 73.0, SD: Not reported	Eight daily saliva samples on two consecutive days: • Awakening • 15, 30, 45 min post-awakening • 3, 6, 9, 12 h post-awakening	Self-reported health and health behaviors; Exclusions: Smoking, heart disease, cancer, psychiatric illnesses, medication such as estrogen, synthetic glucocorticoids, anti-steroid drugs, and anti-seizure drugs that could affect cortisol concentrations	Age, Sex, Time of awakening	Subtracting the 30 min sample from the 12 h post-awakening sample	A timer to separate morning samples
Piazza et al. (2013)	*N* = 1730 (56.53% women) Age range: 33–84 years M_{age} 56.4 SD ± 12.1	Four daily samples on four consecutive days: • Awakening • 30 min post-awakening • Before lunch • Before bedtime	Phone interview about health status; No exclusions for health reported	Sex, Smoking status, Number of chronic health conditions, Medication use, Average cortisol collection time	No slope reported	None
Rueggeberg et al. (2012)	*N* = 122 (50.8% women) Age range: 64–85 years M_{age} 71.61, SD ± 5	Five daily saliva samples on three nonconsecutive, typical days:	Self-reported health and health behaviors; No exclusions for health reported	Age, Sex, Chronic smoking, Chronic illness, BMI,	No slope reported	A timer to separate morning samples, Called to remind about sampling

Study	Participant Characteristics	Cortisol Sampling	Health Screen/Exclusions	Statistical Controls	Slope Calculation Method	Compliance Control
		• Awakening • 30 min post-awakening • 2 pm and 4 pm • Before bedtime		Cortisol-related medication use		
Urry et al. (2006)	*N* = 19 (52.9% women) Age range 62–64 years M_{age}/SD: Not reported	Six daily samples on seven consecutive days: • 30 min post-awakening • Between 9 am and 12 pm • Between 12 pm and 3pm • Between 3 pm and 6 pm • Between 6 pm and 9 pm • Before bedtime	Self-reported health and health behaviors; No exclusions for health reported	None	Regressing log-transformed cortisol values on time for each subject and day	None
Wrosch et al. (2008)	*N* = 184 (51.1% female) Age range: Not reported M_{age} 72.27, SD ± 5.79	Five daily samples on three nonconsecutive, typical days: • Awakening • 30 min post-awakening • 2 pm and 4 pm • Before bedtime	Self-reported health and health behaviors; No exclusions for health reported	Age, Sex, Socioeconomic status	No slope reported	Called to remind about sampling