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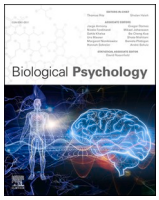

Loneliness, positive social interactions, and diurnal cortisol among mid-to-later life adults in everyday life

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ABSTRACT

Loneliness, the subjective feeling of social isolation, is a major public health concern linked to poor health, including stress-related diseases such as cardiovascular disease. However, less is known about how loneliness relates to biological functioning in everyday life and whether age and social interactions shape these associations. We investigated whether loneliness self-reported in everyday life related to the dynamic range of diurnal cortisol (CDR) compared to other indicators of diurnal cortisol (including the cortisol awakening response [CAR], diurnal cortisol slope [DCS], and area under the curve [AUC]). We also tested whether associations varied by age and frequency of positive social interactions. Data come from a national daily assessment study with participants ranging between 34 and 83 years old who completed 8 days of daily diary assessments (N = 626) and 4 days of salivary cortisol collection. Linear regression analyses showed that people with higher average daily loneliness had more compressed levels of CDR ($b = -2.66$, $SE = 0.74$, $p < .001$), an association that did not differ by age ($b = -0.04$, $SE = 0.06$, $p = .46$). The association between loneliness and CDR varied as a function of the number of days with positive social interactions ($b = 0.90$, $SE = 0.18$, $p = 0.02$), such that the association was smaller among people who reported more positive social interactions. No associations were found for CAR, DCS, or AUC. Findings suggest that greater loneliness in daily life is associated with reduced HPA-axis flexibility, particularly among individuals with fewer positive social interactions.

Loneliness, the subjective feeling of social isolation, is a major public health concern for not only its influence on mental health, but also physical health (US Department of Health and Human Services, 2023). One pathway through which loneliness may contribute to poorer physical health is via heightened activation of the hypothalamic-pituitary-adrenal (HPA) axis, a key component of the stress response system implicated in numerous stress-related diseases. Unlike other negative socio-emotional states (e.g., worry, anger, sadness) that tend to be more context-specific, loneliness reflects a perception of unmet belonging needs and social threat. From an evolutionary perspective, being socially isolated meant greater vulnerability for danger (Cacioppo et al., 2014); thus, even in modern society, the brain interprets loneliness as a social threat, eliciting vigilance and self-preservation. Such a response may be adaptive acutely, but when loneliness is prolonged, the prolonged and repeated activation of the HPA axis in everyday life may lead to blunted HPA-axis functioning and negative health effects. For example, loneliness has been linked to metabolic syndrome, defined as a cluster of factors shown to increase the risk for stress-related diseases and conditions such as cardiovascular disease, diabetes, stroke, and mortality (Whisman, 2010). Researchers posit that the HPA axis plays a prominent role in the pathogenesis of metabolic syndrome (Anagnostis et al., 2009). Further, approximately one third of adults 50 years and older are lonely (Nania, 2024), placing them at risk for stress-related diseases, and nearly half of Americans aged 50 and older meet the criteria for metabolic syndrome (Hirode & Wong, 2020). Together, evidence points to midlife as a critical time to

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assess the impact of everyday loneliness on HPA-axis functioning.

Midlife is a pivotal developmental period that presents significant transitions and shapes health into older age (Lachman et al., 2015). For example, midlife may consist of shifting relationships with children, caregiving for parents, normative health decline, and shifts in social roles and networks— factors that may influence loneliness in everyday life (Antonucci et al., 2014; Infurna et al., 2020; Infurna et al., 2021). HPA axis over-activation due to loneliness increases risk for *allostatic load*, or the buildup of wear and tear on the body over time (McEwen, 2007). The hormone cortisol plays a critical role in regulating the HPA axis (Sapolsky et al., 2000); thus, different metrics of cortisol in everyday life can provide useful information regarding HPA axis functioning. One cortisol metric that may be useful to assess during midlife is the dynamic range of diurnal cortisol (or cortisol dynamic range, CDR), which represents the range of diurnal cortisol levels. Previous research emphasizes the utility of assessing CDR as an indicator of HPA dysregulation due to social adversity during midlife (e.g., Charles et al., 2020; Karlamangla et al., 2019). Further, given the widespread prevalence of loneliness during mid-to-later life, it is not only valuable to investigate associations between loneliness and physiological indicators, but it is also useful to examine factors that may contextualize such associations in everyday life. Past evidence shows that social interactions and events in daily life are linked with well-being (e.g., Bernstein et al., 2018); thus, social engagement in daily life could be important to consider alongside loneliness and HPA-axis functioning in everyday life.

1. Loneliness and cortisol

There are several common indicators of cortisol that provide related, but unique information about HPA-axis regulation in relation to loneliness. The HPA axis releases cortisol throughout the day in a natural diurnal rhythm, with levels peaking shortly after waking (called the cortisol awakening response or CAR) and then gradually decreasing throughout the day (called the diurnal cortisol slope or DCS; Adam & Kumari, 2009; Pruessner et al., 1997). Higher than typical levels of CAR and flatter DCS suggest chronic stress and dysregulation (Stalder et al., 2025; Adam et al., 2006). The total amount of daily cortisol output is referred to as the area under the curve (AUC), with higher levels generally representing chronic activation, and lower levels representing a blunted response (Pruessner et al., 2003). The CDR represents the difference between the expected highest and lowest values of diurnal cortisol and is described in more detail below (Charles et al., 2020).

Several studies have investigated between-person associations between loneliness and different metrics of cortisol; however, few have investigated this association during midlife and older adulthood, and these studies have yielded mixed findings. For instance, Steptoe and colleagues (2004) found that among adults aged 47–59, higher levels of trait-like loneliness (assessed via the UCLA Loneliness Scale; Russell et al., 1980) were linked with a higher CAR, but not with the DCS. In contrast, Johar and colleagues (2021) observed that in a sample of married older adults, loneliness was related to a flatter DCS but showed no association with CAR. Meanwhile, a broader age-range study involving participants aged 25–75 reported no significant associations between loneliness and cortisol levels at waking, CAR, or DCS (Zilioli & Jiang, 2021). Lastly, Schutter et al. (2017) found that among older adults, loneliness was associated with lower AUC within the first hour after waking. Other somewhat related research emphasizes the utility of assessing CDR as an indicator of HPA dysregulation due to social adversity among mid-to-later life adults (e.g., Charles et al., 2020; Karlamangla et al., 2019), yet no research to date has tested whether loneliness relates to CDR. CDR may offer unique and complementary information to other commonly used cortisol metrics (i.e., CAR, DCS, AUC) by capturing *regulatory flexibility* of the HPA axis among midlife adults.

A healthy HPA axis is flexible, responding to stress and recovering appropriately. Greater CDR values represent a more adaptive, flexible stress response system, whereas compressed (smaller) CDR values represent a less-adaptive stress response system and potential HPA-axis dysregulation (Charles et al., 2020; Karlamangla et al., 2022). People with blunted cortisol rhythms may still have normal average levels of daily cortisol. The CDR may help detect these blunted rhythms even when total output (e.g., AUC) appears typical. Further, in comparison to the DCS, which measures the rate of change in cortisol across the waking day, the CDR provides information about the *magnitude* of change that occurs across the waking day. Although DCS and CDR are typically correlated, they provide distinct information about the diurnal pattern of cortisol. An individual can have a relatively healthy DCS but still have a compressed CDR if cortisol levels are lower overall (e.g., not mounting a robust morning response and/or not decreasing effectively at night), which are signs of reduced HPA-axis flexibility. Investigating the association between average daily loneliness and CDR - alongside other common indicators of diurnal cortisol – may clarify where existing findings converge or diverge, thereby helping to explain mixed evidence in the literature.

2. Social Interactions and well-being

Social relationships serve as key regulators of psychological well-being and many physiological functions (Reis et al., 2017). In addition to examining the main association between loneliness and HPA-axis functioning, it may also be helpful to contextualize this association. One potentially useful way of doing this is to consider the occurrence of daily social interactions/events in tandem with the subjective perception of one's social relationships (i.e., loneliness). A vast literature shows the importance of supportive relationships for physiology and health (e.g., Cundiff et al., 2016) and emerging evidence demonstrates the association between social interactions in daily life with well-being. For example, one study of adults (M_{age}= 41.21) found that on average (at the between-person level), people who had more pleasant social interactions generally reported more positive outcomes, including more happiness and less sadness and stress; however, this study did not find a significant association with diurnal cortisol (Bernstein et al., 2018). Another study of adults (M_{age}= 42.86) found that more socially integrated individuals (defined as greater diversity in social engagement over the last 2 weeks) showed steeper cortisol slopes indicating better HPA-axis functioning in daily life (Dickman et al., 2020). Examining both the self-evaluative aspect of loneliness alongside the behavioral aspect of social engagement may help to capture specific facets or subtypes of loneliness most associated with HPA-axis functioning.

3. The current research

The current research builds upon previous studies by examining the link between loneliness and HPA-axis regulation in everyday life. The first aim of the current research is to examine the association between average daily loneliness and CDR and to compare this to other common indicators of cortisol (i.e., CAR, DCS, and AUC). Based on previous evidence linking social adversity to CDR among mid-to-later life adults (e.g., Charles et al., 2020; Karlamangla et al., 2019), we hypothesized that higher average daily loneliness would be associated with a more compressed CDR (i.e., narrower range). Given mixed evidence in the literature, we had no hypotheses about other indicators of cortisol. The second aim of the current research is to examine moderators of this association. We investigate age differences on an exploratory basis to examine whether associations differ for individuals across the broad developmental periods of midlife to older adulthood. Lastly, given theory and prior evidence suggesting that everyday social experiences may provide important context for better understanding well-being, we examined whether the association between average daily loneliness and HPA-axis functioning varied as a function of individuals' positive social interactions in daily life. Specifically, we tested whether the association between loneliness and HPA-axis functioning differed across levels of

positive social interactions, thereby considering the joint contributions of the subjective experience of loneliness and the behavioral dimension of social engagement. We hypothesized that the association between loneliness and CDR would vary across levels of positive social interactions, such that individuals reporting more frequent positive social interactions would exhibit a weaker association between loneliness and CDR.

In the current research, we analyze data that were captured repeatedly in everyday life, which may increase ecological validity and reduce recall bias in self-reports. We aggregated repeated measures and focused on between-person differences to test whether typical levels of daily loneliness are associated with average cortisol metrics across the study period. This approach was conceptually aligned with our aims and hypotheses on individual differences and was also empirically warranted, as loneliness exhibited minimal within-person variability across days in this sample of midlife adults.

4. Method

4.1. Participants and procedures

Data come from Wave 2 of the National Study of Daily Experiences (NSDEII, collected between 2004 and 2009), the daily diary portion of the MIDUS (Midlife in the United States) project.[1] MIDUS is a large-scale longitudinal study that examines biopsychosocial factors of well-being during adulthood. Demographic data was drawn from the main MIDUS Wave 2 Baseline survey. The remainder of the data for the current analyses come from daily phone interviews (eight days), which included a salivary cortisol collection (four times a day, for four days) during the daily diary project portion of the study, as well as a question about their feelings of loneliness (among other self-report variables) each day. Of the 2022 participants included in the NSDEII sample, only those with complete data on all key variables and covariates were included in the current analyses (see below for details on the final sample size). The total analytic sample consisted of 626 adults aged 34–83 years old (55% women, 95% white, 35% with bachelor's degree or higher; see Table 1). Study procedures were approved by The Pennsylvania State University Institutional review board (PRAMS00042558) and the University of Wisconsin, Madison (2016–1051). The privacy rights of human subjects were observed and informed consent was obtained.

5. Measures

5.1. Average daily loneliness

Loneliness was measured daily via self-reports using the single-item question, "How much of the time today did you feel lonely?". Response options ranged from 0 (*none of the time*) to 4 (*all of the time*). Scores were averaged across the 8 days for each person to represent average levels of daily loneliness. Although average daily loneliness was positively skewed, it was modeled as a continuous variable to preserve variability across the full range of reported experiences and avoid loss of information associated with categorizing continuous variables.

5.2. Days with positive social interactions

Positive social interactions were assessed via self-reports in each daily survey with the question, "Did you have a positive interaction with someone?". Responses were coded as 0 (*no*) or 1 (*yes*), and days with positive social interactions were summed to a total number of days participants had positive social interactions across the study period, ranging from 0 to 8. Scores were adjusted for missingness by first calculating the mean number of days with a positive social interaction for each person, then multiplying by the total number of possible day (eight). This puts scores on the scale of eight days, regardless of how many survey days participants completed.

Table 1
Sample Characteristics.

	Range (N = 1277)	Sample with no covariates (N = 1277)	Analytic sample with covariates (N = 626)
Age (Mean ±SD)	33–84	56.04 ± 12.04	55.87 ± 11.80
Gender			
Women (n)		728	339
Men (n)		549	287
Race			
White (n)		1067	588
All other races (n)		86	38
BMI (Mean ± SD)	14.23 – 58.00	27.94 ± 5.69	28.07 ± 5.98
Wake time, hours (Mean ± SD)	8.33 – 19.50	15.82 ± 1.24	15.83 ± 1.21
Psychiatric Medications (n)		182	138
Smoking Status (n)		714	527
Daily Physical Activity Minutes (Mean ± SD)	0–510	39.48 ± 55.00	43.41 ± 60.17
Daily Loneliness (Mean ± SD)	0–4	0.14 ± 0.13	0.15 ± 0.43
Days with Positive Social Interactions (Mean ± SD)	0–8	5.02 ± 2.25	4.87 ± 2.17
Cortisol AUC (Mean ± SD)	0.85 – 464.64	136.23 ± 59.34	140.74 ± 58.20
CDR (Mean ± SD)	-24.75 – 54.24	16.87 ± 9.44	18.09 ± 9.26

Note. Positive social interactions = sum of days with positive social interactions reported across the eight-day study protocol adjusted for missingness; Smoking status (ever been a regular smoker=1 / never been a regular smoker=0)

5.3. Cortisol assessment

Cortisol samples were collected using salivettes from a home saliva collection kit (Sarsedt, Rommelsdorf, Germany) four times per day for four consecutive days. To capture the full diurnal curve of cortisol, saliva samples were collected at waking (T1), 30 min after waking (T2), before lunch (T3), and before bed (T4). Sample collection times were recorded twice, once by participants in a paper-pen journal and again by researchers during nighttime phone interviews for validation. Cortisol concentrations were derived from saliva samples using bioluminescence immunoassays (IBL, Hamburg, Germany), resulting in 26,257 total samples from 2022 individuals. Intra- and inter-assay coefficients of variation were below 5%. Cortisol values were excluded from analyses if they were greater than 60 nMol/L, if the difference between T2 and T3 cortisol values were greater than 10 nMol/L, and on days when participants awakened before 4 AM or after 11 AM (7941 samples removed). In total, 18,022 cortisol samples from 1296 participants were used to calculate CDR (further participants were excluded from the final analytic sample after including covariates in final models, see below for more details).

5.4. Average dynamic range of diurnal cortisol (CDR)

CDR was calculated by subtracting the nadir cortisol values (T4; before-sleep) from the peak cortisol values (T2; 30 min after waking) within each day for each person. Individuals who did not have at least one day with both cortisol assessments (T4 and T2) were excluded from analyses. This resulted in a total of 1277 people before including covariates. Daily CDR values (up to four) were then averaged for each person

[1] For more information on the MIDUS and NSDE study design and to access publicly available data, visit https://midus.colectica.org.

to create a between-person indicator of average CDR across the study protocol. Higher CDR values reflect a greater range in diurnal cortisol (Karlamangla et al., 2022).

5.5. Average cortisol awakening response (CAR)

The CAR was computed by taking the difference between the second cortisol assessment (approximately 30 min after waking) and the first cortisol assessment (waking assessment) on each day (Stalder et al., 2016). These daily indicators of CAR (up to four days) were then averaged within each individual to create a person-specific indicator of average CAR across the study period.

5.6. Average diurnal cortisol slope (DCS)

The DCS was calculated using person-specific regression analyses (Adam et al., 2010, 2017). Linear regressions were estimated for each person on each day, with cortisol values predicted by time since waking. Slopes were estimated from each day (using all assessments throughout the day) and averaged within individuals to create a person-specific indicator of average diurnal cortisol slopes across the study.

5.7. Average area under the curve (AUC)

The AUC for diurnal cortisol was calculated for each person and on each day using the trapz function from the pracma package in R (Borchers, 2023). This approach uses the trapezoidal rule for numerical integration to approximate the AUC of cortisol based on time since waking. These daily cortisol AUCs were then averaged within individuals to create a person-specific indicator of average diurnal cortisol AUC.

5.8. Covariates

Age, gender, smoking status, body mass index (BMI), wake day (hours), daily physical activity, and current psychiatric medications were included as covariates in all analyses due to the potential influence on diurnal cortisol (Karlamangla et al., 2019). In addition, diurnal cortisol AUC was included as a covariate in the final models as recommended by Karlamangla and colleagues (2022). Age was treated as continuous years ranging from 34 to 83. Gender was coded dichotomously (0 = *men*, 1 = *women*) as no other self-report options were available. An indicator for smoking status was created by combining responses to two survey questions: "Do you smoke cigarettes regularly now? (*Yes/No*)" and "Have you ever smoked cigarettes regularly - that is, at least a few cigarettes a day? (*Yes/No*)". A variable indicating whether someone ever smoked regularly was created, with individuals who responded *no* to both questions coded as 0 = *never smoked*, and individuals who responded *yes* to either question coded as 1 = *ever smoked*. Race was dichotomized as 1 = *White*, 0 = *all else*. BMI was computed by dividing weight (kg) by height squared (meters). Average wake day (hours) was created by first calculating wake day in hours for each day based on self-reported wake/bedtime, then averaging daily wake hours across the study protocol (8 days) for each person. Daily physical activity (minutes) was created by averaging the number of self-reported minutes spent engaging in physical activity "that would cause you to break a sweat" each day. Psychiatric medication was coded as currently taking anxiety or depression medication (1 = *yes*, 0 = *no*).

6. Analytic strategy

All data management and analyses were conducted in the R statistical software program (R Core Team, 2024). A series of multiple linear regression models were estimated to evaluate the association between average levels of daily loneliness and CDR, CAR, DCS, and AUC (Aim 1) and whether age or number of days with positive social interactions moderated these associations (Aim 2). The sample size for models before adjusting for covariates included 1277 participants. After the inclusion of covariates in models, the sample size included 626 participants, due to missingness in covariate data.[2]

7. Results

7.1. Preliminary analyses

Participants reported an average level of 0.15 (*SD* =.43) for daily loneliness (scale of 0 – 4) and a mean of 5.02 (*SD* = 2.25) days with positive social interactions across the study period (eight days). There were no significant differences in demographic and psychosocial characteristics between the final analytic sample (N = 626) and the full sample (N = 1277). Information on sample characteristics are presented in Table 1 and correlations among key study variables are presented in Table 2.

7.2. Association between loneliness and different indicators of diurnal cortisol

Higher average daily loneliness was significantly associated with compressed CDR (*b* = −2.66, *SE* = 0.74, 95% CI [-4.11, −1.21]). Specifically, for every 1 unit increase in average daily loneliness, there was a 2.66 unit decrease in CDR. These results were evident with and without covariates. Complete results for adjusted models (with covariates) are presented in Table 3 and unadjusted model results are presented in Supplementary Material. Average daily loneliness was not significantly associated with any other indicators of diurnal cortisol (See Table 4).

7.3. Moderation by age and positive social interactions

Moderation analyses indicated that the association between average daily loneliness and CDR varied as a function of the number of days that positive social interactions were reported (*b* = 0.90, *SE* = 0.38, 95% CI [0.15, 1.65]). Specifically, the positive association between average daily loneliness and CDR was 0.90 units weaker for each added day that positive social interactions were reported (See Fig. 1). Positive social interactions did not significantly moderate the association between average daily loneliness and any other cortisol metric (*ps* >.05; see Supplementary Material). There were no significant differences in the association between average daily loneliness and any cortisol metric by age (See Tables 3 and 5). Complete results for adjusted models (with covariates) are presented in Table 3 and unadjusted model results are presented in Supplementary Material.

8. Discussion

In the current research, we investigated the association between average daily loneliness and the CDR (an indicator of HPA-axis functioning) among mid-to-later life adults in everyday life. More specifically, we examined CDR alongside other common metrics of diurnal cortisol to assess whether findings converged or diverged. In line with our main hypothesis, we found that higher levels of average daily loneliness were associated with a more compressed CDR across the study period. Further, as hypothesized, the association between average daily loneliness and CDR was weaker among individuals who reported more days with positive social interactions, even after adjusting for key demographic and biobehavioral characteristics. We found no significant differences in associations between average daily loneliness and CDR by

[2] A large portion of missingness stemmed from smoking status (n = 429) and psychiatric medications (n = 365). For this reason, we also conducted sensitivity analyses without the inclusion of these covariates and results followed the same pattern (see Table 5 in Supplemental Material).

Table 2
Correlation matrix of key variables.

	CDR	DCS	CAR	AUC	Lonely	Age	Smoke	BMI	Avg Wake	Avg Phys	Woman	White	Psych Meds	PSI Total
CDR	1.00													
DCS	**-0.52**	1.00												
CAR	**0.65**	-0.11	1.00											
AUC	**0.50**	**-0.27**	**0.39**	1.00										
Lonely	-0.10	0.01	-0.06	0.01	1.00									
Age	0.09	-0.02	0.12	0.18	-0.05	1.00								
Smoke	0.04	-0.04	-0.08	-0.03	-0.07	0.16	1.00							
BMI	-0.08	0.06	-0.02	-0.05	0.03	0.00	0.06	1.00						
Avg Wake	0.09	0.04	0.12	0.23	-0.08	-0.07	-0.01	0.02	1.00					
Avg Phys	0.03	-0.05	0.00	0.04	-0.02	-0.01	-0.05	-0.07	0.06	1.00				
Woman	-0.02	0.04	0.11	-0.10	0.01	-0.02	-0.07	-0.04	-0.10	-0.14	1.00			
White	0.05	-0.06	-0.03	-0.03	-0.03	0.01	-0.02	-0.09	-0.06	0.04	0.04	1.00		
Psych Meds	-0.02	0.03	0.03	-0.02	0.18	0.04	-0.08	0.06	-0.16	-0.09	0.15	-0.01	1.00	
PSI Total	0.09	0.00	0.06	0.04	-0.10	0.11	0.15	-0.08	0.04	0.00	0.07	0.06	0.01	1.00

Note: Bolded values indicate statistical significance at $p < .05$; Lonely=Average daily loneliness, Smoke = smoking status (ever been a regular smoker=1 / never been a regular smoker=0); Race: White= 1, all else= 0; CDR=dynamic range of diurnal cortisol; AUC=average cortisol AUC, Avg Wake = average daily time awake (hours); Avg Phys= Average daily physical activity (min); PSI = # of days with positive social interactio

Table 3
Linear regression results of the association between average daily loneliness and the dynamic range of diurnal cortisol, and results of moderation analyses (age, total days with positive social interactions), N = 626.

	Loneliness → CDR					Age Moderation					PSI Moderation				
Coefficients	*b*	*β*	*SE*	CI_{lower}	CI_{upper}	*b*	*β*	*SE*	CI_{lower}	CI_{upper}	*b*	*β*	*SE*	CI_{lower}	CI_{upper}
(Intercept)	**14.03**	-	**5.19**	**3.84**	**24.22**	**13.84**	-	**5.19**	**3.63**	**24.04**	**13.92**	-	**5.17**	**3.76**	**24.07**
Lonely	**-2.66**	-0.12	**0.74**	**-4.11**	**-1.21**	-0.32	-0.01	0.74	-6.66	6.01	**-5.93**	**-0.28**	**1.61**	**-9.10**	**-2.76**
Age	-0.01	-0.01	0.03	-0.06	0.05	-0.00	-0.01	0.03	-0.06	0.05	-0.00	-0.01	0.03	-0.06	0.05
Smoke	1.50	0.06	0.88	-0.23	3.23	1.54	0.06	0.88	-0.20	3.27	1.39	0.05	0.89	-0.36	3.13
Race	0.80	0.02	1.32	-1.79	3.40	0.81	0.02	1.32	-1.78	3.41	1.13	0.03	1.33	-1.49	3.75
BMI	-0.06	-0.04	0.05	-0.17	0.04	-0.06	-0.04	0.05	-0.17	0.04	-0.07	-0.04	0.05	-0.17	0.03
AUC	**0.09**	**0.55**	**0.01**	**0.08**	**0.10**	**0.09**	**0.55**	**0.01**	**0.08**	**0.10**	**0.09**	**0.56**	**0.01**	**0.08**	**0.10**
Avg Wake	**-0.55**	**-0.07**	**0.27**	**-1.08**	**-0.02**	**-0.54**	**-0.07**	**0.27**	**-1.07**	**-0.01**	**-0.60**	**-0.08**	**0.27**	**-1.13**	**-0.07**
Avg Phys	-0.00	0.00	0.01	-0.01	0.01	-0.00	0.00	0.01	-0.01	0.01	-0.00	0.00	0.01	-0.01	0.01
Woman	0.97	0.05	0.66	-0.32	2.27	1.00	0.05	0.66	-0.30	2.29	0.91	0.05	0.66	-0.38	2.20
Psych Meds	-0.20	-0.01	0.78	-1.74	1.34	-0.22	-0.01	0.78	-1.76	1.32	-0.10	0.00	0.78	-1.64	1.44
Lonely x Age						-0.04	-0.11	0.06	-0.15	0.07					
PSI total											0.17	0.04	0.14	-0.11	0.46
Lonely x PSI											**0.90**	**0.18**	**0.38**	**0.15**	**1.65**

*Bolded values indicate statistical significance at $p < .05$
Note: Lonely=Average daily loneliness, Smoke = smoking status (ever been a regular smoker=1 / never been a regular smoker=0); Race: White= 1, all else= 0; CDR=dynamic range of diurnal cortisol; AUC=average diurnal cortisol area under the curve, Avg Wake = average daily time awake (hours); Avg Phys= Average daily physical activity (min); PSI = # of days with positive social interactions.

age. Notably, no significant associations were found with other metrics of diurnal cortisol (CAR, DCS, AUC).

Several studies have examined individual differences in the association between loneliness and cortisol; however, limited studies have examined this association during midlife and older adulthood, and these studies have yielded mixed findings. Prior studies have reported that loneliness is associated with a higher CAR (Steptoe et al., 2004), flatter DCS (Johar et al., 2021) J and lower AUC within the first hour after waking (Schutter et al., 2017). In contrast, null associations have been reported between loneliness and DCS (Steptoe et al., 2004), CAR (Johar et al., 2021; Zilioli & Jiang, 2021), and cortisol at waking and DCS (Zilioli & Jiang, 2021). The current research examined CDR *alongside* other common diurnal cortisol metrics to help clarify which aspects of diurnal HPA-axis activity may relate to mean levels of daily loneliness among midlife adults. These cortisol indices capture distinct features of cortisol dynamics. Whereas AUC reflects overall daily cortisol output and CAR and DCS capture specific dynamic transitions (i.e., the morning rise and daytime decline), CDR reflects the overall scope of the diurnal rhythm across the day. In this context, CDR provides an index of how pronounced the daily cortisol rhythm is across waking hours and has been interpreted as an indicator of broader HPA-axis regulation.

Our finding that higher levels of average daily loneliness relate to a more compressed CDR is consistent with related research linking other forms of social adversity (e.g., childhood adversity, low socioeconomic

Table 4
Comparison of linear regression model results, with loneliness predicting different diurnal cortisol metric outcomes.

	DCS				CAR				AUC			
Coefficient	*b*	β	*SE*	*p*	*b*	β	*SE*	*p*	*b*	β	*SE*	*p*
Intercept	**-1.70**	**-**	**0.46**	**< 0.001**	-3.46	-	5.08	0.50	-28.18	-	37.19	0.45
Lonely	0.09	0.05	0.07	0.21	-1.42	-0.08	0.72	0.05	1.33	0.01	5.30	0.80
Age	0.00	0.01	0.00	0.82	**0.09**	**0.13**	**0.03**	**< 0.001**	**0.79**	**0.16**	**0.19**	**< 0.001**
Smoke	-0.01	0.00	0.08	0.91	**-2.59**	**-0.12**	**0.86**	**0.003**	**-18.05**	**-0.11**	**6.28**	**0.004**
Race	-0.09	-0.03	0.12	0.48	-1.71	-0.05	1.29	0.19	-5.58	-0.02	-0.47	0.56
BMI	0.00	0.04	0.00	0.38	-0.05	-0.04	0.05	0.36	-0.41	-0.04	0.38	0.28
Avg Wake	0.04	0.07	0.02	0.13	**0.57**	**0.09**	**0.26**	**0.03**	**10.24**	**0.21**	**1.89**	**< 0.001**
Avg Phys	0.00	-0.02	0.00	0.66	0.00	-0.01	0.01	0.82	0.01	0.01	0.04	0.72
Woman	0.09	0.07	0.06	0.12	**1.89**	**0.12**	**0.64**	**0.003**	**-12.55**	**-0.11**	**4.70**	**0.008**
Psych Meds	0.04	0.03	0.07	0.56	0.06	0.00	0.77	0.94	4.60	0.03	5.62	0.41

*Bolded values indicate statistical significance at $p < .05$
Note: Lonely=Average daily loneliness, Smoke= smoking status (ever been a regular smoker=1 / never been a regular smoker=0); Race: White= 1, all else= 0; DCS= Diurnal cortisol slope; CAR= cortisol awakening response; AUC= average diurnal cortisol area under the curve, Avg Wake= average daily time awake (hours); Avg Phys= Average daily physical activity (min); PSI = # of days with positive social interactions

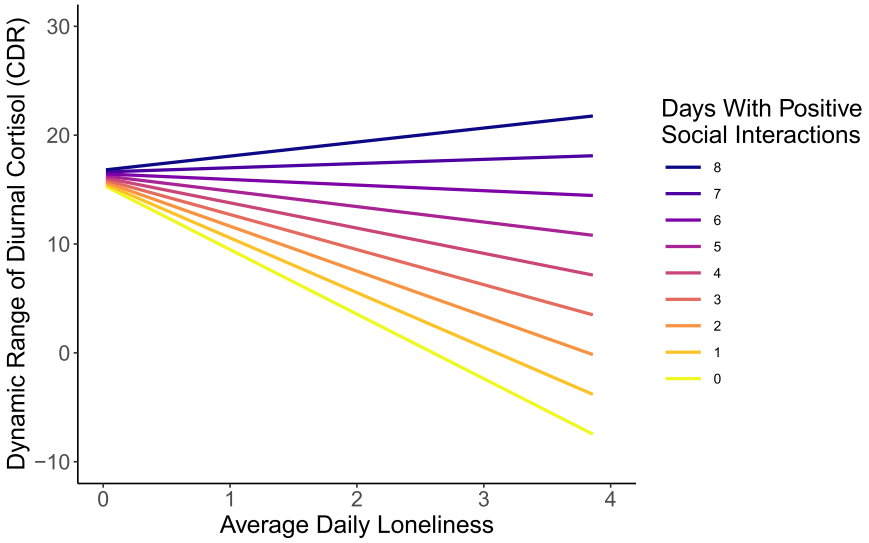

Fig. 1. Plot of the association between average daily loneliness and the dynamic range of diurnal cortisol, moderated by the total number of days with positive social interactions. Note. Each line represents the predicted slope for the given number of days with positive social interactions. The association between average daily loneliness and CDR became progressively smaller as the number of positive social interactions increased and was no longer statistically different from zero among individuals reporting five or more positive social interactions (see Fig. 1 in the Supplementary Materi.

Table 5
Results of moderation analyses – chronological age moderating the association between average daily loneliness and different cortisol metrics.

	DCS				CAR				AUC			
Effect	*b*	β	*SE*	*p*	*b*	β	*SE*	*p*	*b*	β	*SE*	*p*
Intercept	**-1.69**	**-**	**0.46**	**< 0.001**	-3.72		5.09	0.47	-28.63	-	37.27	0.44
Lonely	-0.02	-0.01	0.32	0.96	1.64	0.09	3.16	0.60	6.74	0.05	23.14	0.77
Age	0.00	0.01	0.00	0.84	**0.09**	**0.13**	**0.03**	**< 0.001**	**0.79**	**0.16**	**0.19**	**< 0.001**
Smoke	-0.01	-0.01	0.08	0.89	**-2.54**	**-0.12**	**0.86**	**0.003**	**-17.97**	**-0.11**	**6.29**	**0.004**
Race	-0.09	-0.03	0.12	0.47	-1.70	-0.05	1.29	0.19	-5.56	-0.02	9.48	0.56
BMI	0.00	0.04	0.00	0.37	-0.05	-4.00	0.05	0.35	-0.41	-0.04	0.38	0.28
Avg Wake	0.04	0.07	0.02	0.13	**0.58**	**0.09**	**0.26**	**0.02**	**10.25**	**0.21**	**1.89**	**< 0.001**
Avg Phys	0.00	-0.02	0.00	0.65	0.00	-0.01	0.01	0.85	0.01	0.01	0.04	0.71
Woman	0.09	0.07	0.06	0.13	**1.93**	**0.12**	**0.64**	**0.003**	**-12.49**	**-0.11**	**4.71**	**0.01**
Psych Meds	0.04	0.03	0.07	0.55	0.03	0.00	0.77	0.97	4.54	0.03	5.62	0.42
Age*Lonely	0.00	0.07	0.01	0.73	-0.05	-0.17	0.06	0.32	-0.09	-0.04	0.41	0.81

Note: Lonely=Average daily loneliness, Smoke= smoking status (ever been a regular smoker=1 / never been a regular smoker=0); Race: White= 1, all else= 0; DCS= Diurnal cortisol slope; CAR= cortisol awakening response; AUC= average diurnal cortisol area under the curve, Avg Wake= average daily time awake (hours); Avg Phys= Average daily physical activity (min); PSI= # of days with positive social interactions

status) to compressed CDR during midlife (e.g., Karlamangla et al., 2019), as well as theoretical perspectives suggesting that dysregulation of the HPA axis may be one mechanism linking loneliness to long-term stress-related diseases (Cacioppo & Hawkley, 2009). A compressed, or blunted, cortisol rhythm reflects a reduced distinction between morning peak and lower evening cortisol levels, which has been interpreted as a

marker of prolonged or chronic HPA-axis activation over time.

Importantly, the absence of associations with other cortisol metrics (CAR, DCS, AUC) does not indicate that CDR is inherently a more sensitive or superior measure of HPA-axis functioning. Rather, the pattern of findings may suggest that average daily loneliness relates more closely to the overall shape of the diurnal cortisol rhythm than to total daily cortisol secretion or specific transition periods such as the morning rise or daytime decline. In other words, loneliness may be reflected in the global rhythm of cortisol activity across the day rather than in discrete components of the diurnal cycle. The current findings therefore highlight a potential connection between overall daily feelings about social relationships and broader patterns of physiological regulation. Given a more compressed CDR has been interpreted as an indicator of allostatic load and previous research has linked allostatic load to longitudinal risk for all-cause mortality and cognitive decline (Karlamangla et al., 2022), the current findings raise the possibility that feelings of loneliness in everyday life may be associated with physiological patterns relevant to long-term health during midlife and older adulthood.

There were no significant age differences in the association between average daily loneliness and CDR among the current sample of 34–83 year-olds. Although certain aspects of diurnal cortisol rhythms typically change with healthy aging - such as lower morning peaks and flatter diurnal slopes (Karlamangla et al., 2013; Nater et al., 2013) - the current findings suggest the specific association between loneliness and the CDR (which encompasses the range of cortisol levels across the day) remains relatively stable across adulthood. It is possible that ages outside of the range of 34–83 years (e.g., adolescence or very late-life) are critical windows of distinct differences in the association. Additionally, age-related resilience or vulnerability might be individual difference-dependent such that age differences exist in specific contexts. For example, individuals who are older *and* have limited socioeconomic resources may have stronger associations between loneliness and CDR due to reduced access to psychological, social, or medical resources (Chen & Miller, 2013; Hawkley & Cacioppo, 2010).

Loneliness is a subjective feeling of social isolation regardless of one's social relationships or network; however, social interactions during everyday life may still play an important role in the experience of loneliness. We found that individuals who both felt lonelier and had fewer positive social interactions in daily life showed poorer HPA-axis functioning (compressed CDR), whereas those who felt lonelier but still had plenty of positive social interactions showed less or no such association. This pattern suggests that the physiological correlates of loneliness may depend in part on the broader context of individuals' daily social experiences. Although loneliness reflects subjective perceptions of social disconnection, the frequency of positive interactions in everyday life may capture an additional dimension of social functioning that shapes how loneliness relates to physiological regulation. Positive social interactions often involve emotional support, validation, and moments of belonging (Cohen & Wills, 1985; Taylor, 2011; Uchino, 2006), which may influence whether loneliness co-occurs with patterns of HPA-axis functioning indicative of dysregulation. Taken together, these findings highlight the importance of considering both subjective feelings of loneliness and everyday social experiences when examining links between social disconnection and stress physiology.

One strength of the current study is that by analyzing data collected repeatedly in daily life, we were able to incorporate natural fluctuations in daily loneliness and diurnal cortisol and incorporate these dynamics into our statistical approach, which made our aggregate estimates more reliable, ecologically valid, and less sensitive to recall bias. Despite this strength and others, several limitations should be considered when interpreting results of this study. Although the current data come from a large national study of adults in the United States, the sample is predominantly White, college-educated, and participants generally reported lower levels of daily loneliness. Given low socioeconomic status and higher loneliness increase risk for worse health and well-being outcomes (Chen & Miller, 2013; Hawkley & Cacioppo, 2010), future research is needed to investigate these associations in diverse samples that may have higher average levels of daily loneliness. Relatedly, the current findings characterize continuous individual differences in loneliness and HPA axis functioning. Consistent with this dimensional perspective, the findings suggest that the association between loneliness and HPA-axis functioning varies across the range of individuals' daily positive social experiences. Future research is needed to determine clinically meaningful thresholds for specific risk classification. Additionally, this study was not designed to detect causal effects; thus, directionality cannot be determined. Finally, the current study provided sufficient data to capture reliable between-person differences in associations. Future studies are needed to investigate within-person associations between daily loneliness and different cortisol metrics (e.g., cortisol functioning on days when loneliness is higher or lower than typical for individuals). Such research will add to the growing knowledge of how the associations examined in the current research function as dynamic individual processes unfolding in daily life.

9. Conclusion

Loneliness is a major public health concern that warrants continued investigation into causes, correlates, and biobehavioral mechanisms linking loneliness to poor health. Our examination showed that individuals who reported higher average daily loneliness exhibited a more compressed dynamic range of diurnal cortisol (CDR) (an association that did not differ by age) among a mid-to-later life sample of adults. The current findings suggest that dysregulation of the HPA axis could be a potential mechanism linking loneliness to long-term stress-related diseases and outcomes. We also found that individuals who both felt lonelier and had fewer positive social interactions in daily life showed poorer HPA functioning (i.e., compressed CDR), whereas those who felt lonelier but still had plenty of positive social interactions showed less or no such association. These findings underscore the importance of social connection and everyday interpersonal experiences and suggest that further research is warranted to inform interventions aimed at mitigating the physiological toll of loneliness.

CRediT authorship contribution statement

Karina Van Bogart: Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Conceptualization. **Almeida David M:** Writing – review & editing, Supervision, Funding acquisition, Data curation. **Felt John M:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis. **Jonathan Rush:** Writing – review & editing. **Cerino Eric:** Writing – review & editing. **Charles Susan T:** Writing – review & editing, Supervision.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors declare they did not use generative AI or AI-assisted technologies in the writing or analyses included in this manuscript.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.biopsycho.2026.109247.

Data availability

Data are publicly available.

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