

Loneliness Is a Unique Predictor of Age-Related Differences in Systolic Blood Pressure

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A population-based sample of Caucasians, African Americans, and Latino Americans, 50–68 years of age ($M = 57.5$), from Cook County, Illinois ($N = 229$), was tested to examine how loneliness and co-occurring psychosocial factors (depressive symptoms, perceived stress, social support, and hostility) were related to indices of cardiovascular and endocrine functioning. Extending prior research, the authors found that loneliness was associated with elevated systolic blood pressure (SBP) and age-related increases in SBP, net of demographic variables, health behavior variables, and the remaining psychosocial factors. Loneliness was not associated with differences in autonomic or endocrine functioning. Although the results are limited by the cross-sectional methods used, they are consistent with the hypothesis that cardiovascular disease contributes to increased morbidity and mortality among lonely individuals.

Keywords: loneliness, blood pressure, age, psychosocial stress

Loneliness, an emotional state that has been described as “a gnawing... chronic disease without redeeming features” (e.g., Weiss, 1973, p. 15; see also Peplau, Russell, & Heim, 1979), afflicts approximately 20% of Americans (Rubenstein & Shaver, 1982; Steffick, 2000). The experience of loneliness includes feelings of isolation (e.g., the absence of or psychological distance from a significant other), feelings of disconnectedness (e.g., feeling one has no confidant or close friends), and feelings of not belonging (e.g., not identifying with or being accepted by salient social groups). Social isolation tends to promote feelings of loneliness, but loneliness is more closely related to qualitative than quantitative aspects of social encounters (Hawkey, Burleson, Berntson, & Cacioppo, 2003; Russell, 1982; Russell, Peplau, & Cutrona, 1980; Wheeler, Reis, & Nezlek, 1983). Of importance, loneliness has been associated with a wide range of problems in middle-aged and older adults including lack of independent living (e.g., Russell, Cutrona, de la Mora, & Wallace, 1997), alcoholism (Akerlind & Hornquist, 1992; Bell, 1956), depressive symptoms

(cf. Russell, 1982; Shaver & Brennan, 1991), impaired immune function (Pressman et al., in press), elevated blood pressure (Cacioppo, Hawkey, Crawford, et al., 2002), impaired sleep (Cacioppo, Hawkey, Berntson, et al., 2002; Cacioppo, Hawkey, Crawford, et al., 2002), and suicide (Goldsmith, Pellmar, Kleinman, & Bunney, 2002; Wenz, 1977).

To date, the bulk of research on perceived social connections and aging or perceived social connections and health has focused on social support rather than loneliness. A Medline search on the combined terms of *social support* and *aging-aged*, for instance, produced 5,714 hits, whereas a Medline search on the combined terms of *loneliness* and *aging-aged* produced 474 hits, only 8% of the number found for social support. The same ratio (approximately 10:1) is found in Medline searches of the combined terms of *social support* and *health* versus *loneliness* and *health*. The constructs of loneliness and social support are related and may tend to be treated as synonymous. In recent years the construct of loneliness has begun to attract attention, however, because (a) conceptual and empirical distinctions between loneliness and social support have been clarified and (b) studies of loneliness have revealed associations and effects that are not evident from the perspective of social support (e.g., Cacioppo et al., 2000, Cacioppo, Hughes, Waite, & Hawkey, in press; Russell et al., 1997; Steptoe, Owen, Kunz-Ebrecht, & Brydon, 2004). For instance, Russell et al. (1997) examined the relation between loneliness and the subsequent admission to a nursing home in a sample of 3,097 individuals ages 65 years or older residing in two rural counties in Iowa. Russell et al. (1997) also considered whether the association between loneliness and nursing home admission could be explained in terms of low social support, demographic characteristics, morale of participants, cognitive status, or physical health status. Among the covariates, age, income, education, prior admis-

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sion to a nursing home, cognitive status, self-rated health, and morale (a composite measure of depressed affect, anxiety, and life satisfaction) significantly predicted nursing home admissions. Net of these covariates, the results demonstrated that individuals whose baseline loneliness scores fell into the highest group were more likely to be admitted to a nursing home over the subsequent 4-year period. Social support, in contrast, was not a significant predictor. Similarly, recent work has revealed that loneliness rather than social support uniquely predicts depressive symptoms (Cacioppo, Hughes, et al., in press).

Loneliness is not solely a mental health problem, however. Reports of chronic illnesses and self-rated physical health have shown associations with loneliness among older adults (Russell, 1996). Moreover, in longitudinal studies, loneliness has predicted mortality in older adults (Penninx et al., 1997; Seeman, 2000; Sugisawa, Liang, & Liu, 1994). For instance, Sugisawa et al. found that the significant effects of loneliness on mortality over a 3-year period were explained by associations between loneliness and chronic diseases, functional status, and self-rated health. Penninx et al. showed that loneliness and a low sense of mastery predicted mortality during a 29-month follow-up net of age, sex, chronic diseases, alcohol use, smoking, self-rated health, and functional limitations.

The primary cause of morbidity and mortality in industrialized nations is cardiovascular disease (e.g., coronary artery disease, left ventricular hypertrophy, and congestive heart failure), and hypertension is a potent risk factor for these diseases (Kannel, 1996). Evidence from prior research suggests that loneliness is associated with elevated systolic blood pressure (SBP) and may contribute to the development of hypertension. First, we found that loneliness was related to differential regulation of SBP in young adults: Although lonely and nonlonely individuals did not differ in blood pressure levels, maintenance of blood pressure was attributable to higher vascular resistance and lower cardiac output among lonely relative to nonlonely individuals (Cacioppo, Hawkey, Crawford, et al., 2002; Hawkey et al., 2003). Increased vascular resistance contributes to the development of essential hypertension, and the structural vascular changes that ensue augment increases in blood pressure (Staessen, Wang, Bianchi, & Birkenhaeger, 2003). This mechanism may serve to accelerate age-related increases in SBP among lonely individuals. Indeed, we subsequently found age-related differences in SBP among lonely but not among nonlonely older adults ($M_{\text{age}} = 65$) living in a condominium in Chicago (Cacioppo, Hawkey, Crawford, et al., 2002). The latter finding was from a small convenience sample, however, and in the current study, we sought to replicate the Age \times Loneliness association with SBP in a larger, population-based sample of middle-aged and older adults.

The sympathetic nervous system (SNS) plays an important role in regulating blood pressure (Christou et al., 2005). The autonomic branch of the SNS contributes to vasomotor tone via the alpha-adrenergically mediated vasoconstriction effects of norepinephrine (NEPI) released at the resistance vessels. Activation of the SNS also elicits the release of epinephrine (EPI) from the adrenal medulla. Although of less importance than NEPI to blood pressure regulation, high concentrations of EPI have an alpha-adrenergic vasoconstrictive effect like that of NEPI. Increased frequency, intensity, or duration of elevated SNS activity, as may be seen in response to intense repeated or chronic stressors, also results in

elevated levels of circulating EPI and NEPI (i.e., that portion of NEPI not taken up at the presynaptic terminal) that contribute to the development of disease (McEwen, 1998; Rozanski, Blumenthal, & Kaplan, 1999). Moreover, overnight urinary excretion rates of either of these catecholamines have been shown to predict mortality and functional decline (Reuben, Talvi, Rowe, & Seeman, 2000). To test whether loneliness is associated with increased SNS activity, we used overnight urinary excretion of EPI as an integrated assessment of prior adrenomedullary activity, and excretion of NEPI as an integrated assessment of prior SNS activity that largely reflects neurotransmitter release at nerve endings.

To the extent loneliness is associated with differential activation of the SNS, the effects may also be evident in cardiac functioning. In our study of young adults, neither sympathetic (i.e., preejection period; PEP) nor parasympathetic (e.g., respiratory sinus arrhythmia; RSA) neural activity at the heart differentiated lonely from nonlonely individuals (Cacioppo, Hawkey, Crawford, et al., 2002). A lack of cardiac effects in young adults does not mean that cardiac processes do not play a role in loneliness-related morbidity and mortality, however. Prolonged elevations in blood pressure result in structural changes in the myocardium (e.g., left ventricular hypertrophy) and compensatory changes in sympathetic neural outflow that may not become evident in cardiac functioning (e.g., contractility) until older age. Thus, we examine whether sympathetic and vagal activity at the heart, as indexed by PEP and RSA, differ as a function of loneliness in our sample of middle-aged and older adults.

Stress-related increases in SNS activity are often accompanied by increased activity of the hypothalamic–pituitary–adrenocortical (HPA) system. Glucocorticoids (e.g., cortisol), although critical for metabolism and regulation of immune function, have been associated with the development and/or exacerbation of hypertension (Van Uum, Lender, & Hermus, 2004; Whitworth, Brown, Kelly, & Williamson, 1995), diabetes, depressive symptomatology, and cognitive decline (McEwen, 1998). Loneliness has been associated with alterations in the activity of the HPA system, as was shown by Kiecolt-Glaser et al. (1984), for example, who reported higher levels of urinary cortisol in lonely than nonlonely psychiatric inpatients. More recently, Steptoe et al. (2004) found that lonely individuals showed a greater 30-min postawakening increase in salivary cortisol, and Pressman et al. (in press) found that loneliness was associated with higher early morning and late night levels of circulating cortisol in young adult university students. In the present study, we tested whether loneliness is related to individual differences in HPA activity in a population-based sample of middle-aged and older adults. We used overnight urinary excretion of cortisol to evaluate cumulative HPA activity during the prior day.

Related Psychological Risk Factors

Past research has shown that, relative to nonlonely individuals, lonely individuals report greater depressive symptomatology, hostility, and perceived stress, and poorer social support (reviewed in Ernst & Cacioppo, 1999). Recently, we found that loneliness, when manipulated via hypnotic suggestion, produces changes in these psychosocial factors (Cacioppo, Hawkey, et al., in press). These data suggest that loneliness operates as a central trait, central in the sense that changes in loneliness carry changes in a constel-

lation of related psychosocial factors. This is not to say that loneliness cannot be a consequence of changes in these psychosocial factors. Indeed, loneliness and depressive symptoms appear to be reciprocally and causally related over a 3-year time period (Cacioppo, Hughes, et al., in press).

What is less clear is whether associations between loneliness and physiology reflect something unique to loneliness, or whether these associations reflect “generic” stress as might be evident in any and/or all of the loneliness-related psychosocial factors. This latter explanation for loneliness effects is based on the historic and traditional model of stress, in which all stress is held to be equivalent (e.g., McEwen, 1998; Selye, 1956). According to this model, loneliness, depressive symptoms, perceived stress, poor social support, and hostility are simply alternative manifestations of stress, and their effects on physiology are expected to be indistinguishable. The former explanation, that loneliness is unique in its effects on physiology, represents an alternative conceptualization of psychosocial factors in which different factors are hypothesized to have relatively specific physiological effects. The specificity approach has been used in the study of psychosocial factors to show, for example, that components of Type A behavior (e.g., hostility) are superior to a global measure of Type A behavior in explaining mental and physical symptoms (Edwards & Baglioni, 1991) and predicting coronary heart disease (Booth-Kewley & Friedman, 1987; Matthews & Haynes, 1986). In an extension of this work, Yan et al. (2003) examined a broader range of psychosocial factors and found that time urgency–impatience and hostility were unique prospective predictors of hypertension independent of anxiety and depressive symptoms. Unfortunately, loneliness was not included in their analysis.

We built on this work in several ways. First, we examined whether the association between loneliness and SBP is unique to loneliness or is attributable to (or redundant with) the association between SBP and hostility, depressive symptoms, perceived stress, and/or poor social support. We hypothesized the former based on our prior work. Specifically, lonely individuals differ from non-lonely individuals in their tendency to perceive stressful circumstances as threatening rather than challenging and to passively cope with stress by failing to solicit instrumental and emotional support and by withdrawing from the stress rather than by actively coping and attempting to problem solve (Cacioppo, Hawkley, Crawford, et al., 2002; Hawkley et al., 2003). Threat perceptions and passive coping have each been associated with distinct patterns of cardiovascular activity favoring vascular over myocardial activation (Tomaka, Blascovich, Kelsey, & Leitten, 1993; Sherwood, Dolan, & Light, 1990), which we reasoned would contribute to increased SBP over time (Cacioppo, Hawkley, Crawford, et al., 2002; Hawkley et al., 2003). The adverse effects of stress and coping strategies were evident in elevated total peripheral resistance but not in the regulated physiological end point of resting SBP in lonely young adults, but the best test of this hypothesis is in the aging adult, who has a less resilient physiology and is increasingly likely to show the effects of stress on physiology. This rationale, and our preliminary finding from a small convenience sample showing that age was associated with elevated SBP in lonely but not in nonlonely older adults (Cacioppo, Hawkley, Crawford, et al., 2002), led to our population-based study to test the hypothesis that loneliness is a predictor of “normal” age-related SBP differences.

Second, we examined whether the associations between loneliness (and the related psychosocial factors) and blood pressure reflect an association with general physiological stress responses (autonomic and neuroendocrine) or whether the associations are more nuanced, with specific psychosocial factors uniquely predicting specific physiological responses. The traditional stress model holds that these associations should be general, whereas research on specific psychosocial factors and physiological outcomes suggests otherwise. For example, perceived stress and hostility tend to be associated with elevated cortisol (Goldman et al., 2005; Pope & Smith, 1991), whereas some forms of depression (i.e., atypical depression) are associated with diminished cortisol levels (Levitan, Vaccarino, Brown, & Kennedy, 2002). In the present research, we examined whether the associations between loneliness (as well as the related psychosocial factors of depressive symptomatology, perceived stress, hostility, and social support) reflect a more general association with physiological indices of stress (e.g., catecholamines, cortisol) or whether these associations are nuanced.

Method

Participants

Data for this study were collected in the 1st year of the Chicago Health, Aging, and Social Relations Study (CHASRS), a longitudinal, population-based study of persons born between 1935 and 1952. The target population was non-Hispanic Caucasian, African American, and non-Black Latino American persons between the ages of 50 and 68 living in Cook County, IL, who were English-speaking and sufficiently ambulatory to come to the University of Chicago for a daylong visit to the laboratory. The sample was selected using a multistage probability design in which African Americans and Latino Americans were oversampled and gender equality maintained. First, a sample of households was selected; then, sampled households were screened by telephone for the presence of an age-eligible person. Age-eligible persons were then asked to participate in the study. If a household contained more than one age-eligible person, the person with the most recent birthday was selected. A quota sampling strategy was used to achieve an approximately equal distribution of respondents across the six gender by race–ethnic group combinations. The response rate among eligible persons was 45%, comparable to those for other well-conducted telephone surveys.¹

The final sample size for Year 1 of CHASRS is 229. Demographic characteristics of this sample are provided in Table 1. Participants were paid \$126 for participating in the 1st year.

Procedure

Prior to participants' scheduled day in our laboratory, they were mailed a urine collection bottle containing preservative (50% vol/vol acetic acid). Enclosed in the package were urine collection instructions that asked participants to thoroughly void, but not into the container, before going to bed the night before the laboratory tests. The container was to be used for any nighttime voiding and for the first morning void the next day.

Participants arrived at the laboratory between 8 a.m. and 9 a.m., whereupon the urine sample volume was measured and aliquots of urine were frozen at -80°C and batched for later testing. Participants provided informed consent and then began a day of assessments that included

¹ This response rate assumes that households for which the presence of an eligible individual was unknown (23% of all households) were just as likely to contain an eligible individual as households that were successfully screened.

Table 1
Characteristics of the Chicago Health, Aging, and Social Relations Study Sample (N = 229)

Characteristic	<i>M</i>	<i>SD</i>	%
Age (years)	57.5	4.4	
Female			52.4
Ethnicity			
White			35.8
African American			35.4
Latino American ^a			28.8
Education (years)	13.3	3.0	
Median household income (\$)	65,781	54,959	
Marital status			
Married-cohabiting			61.1
Widowed			9.2
Divorced-separated			24.5
Never married			5.2

^aThe majority of these 66 individuals are Mexican (72%), with the remaining individuals representing a wide range of ethnicities (e.g., Puerto Rican, Cuban, Chilean, Colombian, Dominican, etc.).

standard psychological surveys, interviews, lunch, and a cardiovascular protocol. All psychological measures reported in this article were obtained in the first survey packet completed by participants.

Cardiovascular activity was measured prior to lunch for all participants. Experimenters attached sensors for electrocardiograph, impedance cardiograph, and blood pressure recording. Participants were then seated in a comfortable padded chair (a "recliner" in the full upright position). During a 15-min adaptation period, participants completed questionnaires while experimenters established good signal quality. Participants then sat quietly for an additional 5 min prior to recording baseline cardiovascular activity. Cardiovascular activity was recorded during an orthostatic stress protocol that consisted of a 2-min sitting epoch, followed by a 4-min standing epoch, and ending with another 2-min sitting epoch. A 2-min adaptation period followed each postural change before recording commenced.

Cardiovascular Measures

A Colin Vital Statistics Monitor (model BP-508; Vital Signs, Minster, OH) was used to obtain systolic, diastolic, and mean arterial blood pressure readings from the nondominant arm, which was supported at heart level by a cushion resting on the arm of the participant's chair. The Colin monitor records a pulse wave tonometrically by partial occlusion of the radial artery against the radius at the wrist, allowing for beat-to-beat measurement of blood pressure. The tonometer was calibrated against an initial blood pressure reading obtained using an oscillometric cuff and was periodically recalibrated either automatically or on experimenter initiation.

The electrocardiogram (EKG) was obtained using the standard lead II configuration. The impedance cardiogram was obtained using four sets of dual spot sensors (VerMed, Bellows Falls, VT), two sets on the neck (one pair aligned below each ear) and two sets on the thorax (one pair aligned below the armpit just below the level of the sternum). The EKG and basal thoracic impedance (Z_0) were measured using a Biopac MP100 system (ECG100 and EBI100 modules, respectively; Biopac Systems, Inc., Santa Barbara, CA). EKG, Z_0 , and tonometric blood pressure signals were digitized at 1000 Hz.

Custom software (Mindware, Lafayette Instruments) was used to generate the dZ/dt waveform (i.e., the first derivative of Z_0) necessary to obtain impedance-derived measures (i.e., PEP). The same software was used to verify, edit, and summarize cardiovascular data. For each subject, beat-by-beat measures of SBP and diastolic blood pressure (DBP) were averaged for each minute. We focus on SBP based on recommendations by Choba-

nian et al. (2003), who reported that SBP is superior to DBP in predicting cardiovascular disease, especially in adults over the age of 50 years (Franklin et al., 1997). Heart rate (HR) and interbeat intervals (IBIs) were derived from the EKG signal, and estimates of RSA were obtained using a spectral analysis (fast-Fourier transform) of IBIs for individual minutes. Similarly, EKG and impedance data were ensemble averaged for each minute to produce estimates of the PEP. PEP was quantified as the time interval in milliseconds from the onset of the EKG Q-wave to the B-point of the dZ/dt wave. Minute-by-minute means were then averaged across minutes within posture to increase reliability.

In the following analyses, we focus on cardiovascular activity averaged across 4 min in a seated posture. Six participants were missing SBP. Four were missing HR, 9 were missing RSA, and 44 were missing PEP (primarily due to difficulty obtaining and/or interpreting impedance waveforms in these middle-aged and older adults). The means and standard deviations for SBP, HR, RSA, and PEP are shown in Table 2.

Urinary Measures

Urinary catecholamines (EPI and NEPI), cortisol, and creatinine assessments were conducted using high-performance liquid chromatography (HPLC). The acidity of each urine sample was adjusted as necessary to achieve optimal extraction of constituents. Inter- and intra-assay variabilities (i.e., coefficients of variation) for these HPLC analyses were 4% to 7% for EPI, 3% to 5% for NEPI, 6% to 10% for cortisol, and 2% for creatinine. EPI values below the detectable limit (0.05 ng/ μ l; 19 participants) and cortisol values below the detectable limit (1.0 ng/ μ l; 20 participants) were assigned a value of zero. We received urine samples from 219 of the 229 participants, indicating good adherence to our urinary collection protocol in a population-based sample of middle-aged and older adults.

Creatinine standardization of hormone levels is typically used to correct for hydration and urinary volume differences that could bias estimates of hormone concentration. Creatinine production is also influenced by muscle mass differences, however. We used an impedance system (model BIA-1010; RJL Systems, Clinton Township, MI) to evaluate body composition and calculate the percentage of body weight that was attributable to lean muscle mass. Lean mass was regressed on creatinine concentrations to generate residual creatinine values (deviations from the regression line) representing the amount of creatinine not related to muscle mass. These residuals were then regressed on urinary hormone concentrations to pro-

Table 2
Means and Standard Deviations of Predictor and Criterion Variables

Measure (range of scores or units)	<i>n</i>	<i>M</i>	<i>SD</i>
Loneliness (UCLA; 20–80)	225	36.0	9.8
Depressive symptoms (CES-D-ML ^a ; 0–56)	223	9.8	8.4
Perceived stress (PSS; 0–40)	223	13.3	6.4
Social support (ISEL; 4–16)	218	12.9	2.2
Hostility (CMHo; 0–50)	212	17.4	7.7
Systolic blood pressure (mm Hg)	223	130.6	19.6
Heart rate (beats per minute)	225	65.5	19.6
Respiratory sinus arrhythmia (ms ²)	220	4.92	1.26
Preejection period (ms)	185	103.6	22.1
Urinary epinephrine (nmol/mmol creatinine)	216	0.82	0.64
Urinary norepinephrine (nmol/mmol creatinine)	219	19.8	9.4
Urinary cortisol (nmol/mmol creatinine)	219	4.0	3.6

Note. UCLA = Revised UCLA Loneliness Scale; CES-D-ML = Center for Epidemiologic Studies—Depression scale with loneliness item removed; PSS = Perceived Stress Scale; ISEL = Interpersonal Support Evaluation List; CMHo = Cook-Medley Hostility Scale.

^aScores represent a sum of all items on the CES-D after removal of the loneliness item.

duce residual (creatinine- and muscle-mass-corrected) hormone levels (Masi, Rickett, Hawkley, & Cacioppo, 2004). Residualized hormone levels used in analyses are expressed in nanograms per deciliter of urine. Table 2 displays means and standard deviations of raw urinary hormone concentrations in nmol/mmol creatinine.

Psychological Measures

Revised UCLA Loneliness Scale (R-UCLA). The R-UCLA (Russell, 1996) has been shown to possess construct validity (Russell et al., 1980) as a measure of general loneliness and degree of satisfaction with one's social network. Examples of the items are "I lack companionship" and "I feel in tune with the people around me." Each of the 20 items is rated on a scale with response options 1 (*never*), 2 (*rarely*), 3 (*sometimes*), and 4 (*often*). Cronbach's alpha across all 20 items was .91 in this sample. After reverse scoring appropriate items, loneliness scores were calculated by summing all items. The range of possible scores was 20 to 80, with higher scores signifying greater loneliness. Four participants were missing information on the R-UCLA. The mean and standard deviation for this variable are shown in Table 2.

Center for Epidemiologic Studies—Depression scale (CES-D). The CES-D (Radloff, 1977) is a 20-item self-report questionnaire that assesses depressive feelings and behaviors experienced during the past week. Radloff (1977) reported good psychometric properties of this scale. In our sample, Cronbach's alpha was .89. Responses to each item were recorded using a 4-point Likert-type scale that ranged from 0 (*rarely or none of the time*) to 3 (*most or all of the time*). One item in the CES-D asks whether the respondent felt lonely, so this item was deleted prior to calculating total score on the CES-D to ensure any prediction of depressive symptomatology by loneliness was not due to item overlap. We refer to this total score as CES-D-ML. A depressive symptoms score was computed by summing the responses to the remaining 19 items, yielding a scale score range of 0 (low depressive symptoms) to 56 (high depressive symptoms). Six participants were missing information on the CES-D-ML. The mean and standard deviation for this variable are shown in Table 2.

Perceived Stress Scale (PSS). The PSS (Cohen, Kamarck, & Mermelstein, 1983) is a 10-item self-report questionnaire that asks participants to indicate how often they felt or thought a certain way during the past week (see <http://www.psy.cmu.edu:16080/~scohen> for item content and scoring instructions). Cronbach's alpha across the 10 items was .84. Responses to each item were recorded using a 5-point Likert-type scale that ranged from 0 (*never*) to 4 (*very often*). Scale scores for each participant were calculated by summing the responses to all items, yielding a scale range of 0 (low perceived stress) to 40 (high perceived stress). Six participants were missing information on the PSS. The mean and standard deviation for this variable are shown in Table 2.

Interpersonal Support Evaluation List (ISEL). The ISEL (Cohen & Hoberman, 1983; Cohen, Mermelstein, Kamarck, & Hoberman, 1984) consists of 12 statements to which participants responded on a 4-point Likert-type scale ranging from 1 (*definitely false*) to 4 (*definitely true*; see <http://www.psy.cmu.edu:16080/~scohen> for item content and scoring instructions). Cohen and Hoberman (1983) and Cohen et al. (1984) have provided a discussion of scale design and psychometric properties. In our sample, Cronbach's alpha across the 12 items was .87. In this self-report questionnaire, participants are asked to rate how truly each item reflects their own feelings on a 4-point Likert-type scale that ranges from 1 (*definitely true*) to 4 (*definitely false*). After reverse scoring appropriate items, subscale scores were calculated for appraisal support (e.g., "There is someone I can turn to for advice about handling problems with my family"), belonging support (e.g., "If I wanted to have lunch with someone, I could easily find someone to join me"), and tangible support (e.g., "If I were sick, I could easily find someone to help me with my daily chores"). For the purposes of this study, an overall social support score (range = 4–16) was computed by averaging the subscale scores. Eleven participants

were missing information on the ISEL. The mean and standard deviation for this variable are shown in Table 2.

Cook–Medley Hostility Scale (CMHo). The CMHo (Cook & Medley, 1954) is a 50-item scale developed from the MMPI. In our sample, Cronbach's alpha across the 50 items was .85. For each item, participants were asked to read the accompanying statement and indicate whether or not it applied to them by marking either *true* (1) or *false* (0). After reverse scoring appropriate items, responses were summed to generate a hostility score for each participant. Scores ranged from 0 (low hostility) to 50 (high hostility). Seventeen participants were missing information on the CMHo. The mean and standard deviation for this variable are shown in Table 2.

Covariates

Demographic covariates were gender, ethnicity, age, education (years of schooling), and household income. Household income was reported in 12 categories ranging from less than \$5,000 to more than \$200,000; to achieve a more continuous distribution, we used the log-transformed median of each category in analyses. Missing values for education (2) and household income (13) were replaced with means for the corresponding gender by ethnic group combination. Marital status was dichotomized for the purposes of analysis, with married-cohabiting individuals contrasted with all other marital status categories.

Body mass index (BMI, calculated as weight in kg/(height in m)², served as a covariate in analyses of cardiovascular variables and urinary hormones (Hansen, Garde, Christensen, Eller, & Netterstrøm, 2001; Lee et al., 2001). For cardiovascular variables, additional covariates added because they are known cardiovascular risk factors included alcohol consumption (average number of drinks per day during last 3 months), smoking status (number of packs of cigarettes per day), and blood pressure medications (yes–no). Blood pressure medications were categorized as vasoactive (i.e., alpha-2 agonists, alpha blockers, ACE inhibitors, angiotensin receptor blockers, calcium channel blockers, beta blockers) and volume active (i.e., diuretics). Forty percent of participants were on vasoactive medications, 5% were on volume active medications, and an additional 11% were on both types of medication. Binary logistic regression analyses showed that the likelihood of being on a blood pressure medication did not differ as a function of any of the psychosocial factors ($ps > .2$). However, psychosocial factors such as loneliness and social support may influence participants' likelihood of complying with medication regimens. The addition of blood pressure medications as a covariate avoids spuriously attributing SBP variance to the psychosocial factors themselves rather than to the effects of medication use. Conversely, the absence of a bivariate relationship between SBP and any of the psychosocial factors may reflect a suppression of a real relationship if the psychosocial factor and medication use are confounded (e.g., if lonely individuals take blood pressure medications and nonlonely individuals do not). Holding blood pressure medications constant permits an assessment of the independent effects of the psychosocial factors.

Data Analysis

Ordinary linear regression analyses were used to test the magnitude of the effects of predictor variables on cardiovascular and urinary hormone levels. All psychological predictor variables (i.e., R-UCLA, CES-D-ML, PSS, ISEL, and CMHo) were standardized to a mean of 0 and a standard deviation of 1 in order to represent potentially substantive individual differences in these psychosocial characteristics. Demographic and control variables were kept in original units of measurement. We report unstandardized coefficients throughout, which are therefore interpretable as the magnitude of change in the raw score of the criterion variable associated with a 1-standard-deviation increase in each psychosocial predictor, and with a 1-unit increase for each demographic and control variable.

Among the cardiovascular and urinary hormone variables, no one variable was missing more than 5% of the values (with the exception of PEP,

where poor quality data due to technical difficulties resulted in a larger proportion of missing values). However, the union of all variables used in any one analysis sometimes resulted in larger numbers of missing values. Consequently, we created a dummy variable for persons who did (1) and did not (0) have complete data for the analyses involving any given outcome variable. The dummy variable was therefore treated as a covariate to hold constant any systematic differences between participants with and without complete data. For each criterion measure, the first set of analyses examined first-order correlations between each of the psychosocial factors and the outcome variable. This was followed by a set of linear regression models in which covariates were added to the regression equation to test the individual associations between each of the psychosocial factors and cardiovascular and hormonal criteria independent of demographic characteristics (age, gender, ethnicity, marital status, education, household income) and other covariates known to influence the outcome measure. Loneliness, depressive symptoms, stress, social support, and hostility were significantly intercorrelated, $|r| = .33$ to $.72$, $ps < .001$ (see Table 3). Therefore, all psychological predictors (and covariates) were entered simultaneously in the final model to test the unique effects of each predictor independent of the remaining related psychological predictors. Finally, in the case of SBP, we added an Age \times Loneliness interaction term to replicate the Age \times Loneliness interaction observed in our earlier studies of older adults (Cacioppo, Hawkley, Crawford, et al., 2002). Age was mean-centered in this analysis to enable meaningful interpretation of regression coefficients. Each analysis was based on all available data, and incomplete data were coded using the dummy variable just described.

Results

Cardiovascular Outcomes

SBP. Extending previous findings, a correlational analysis showed that loneliness was associated with higher levels of SBP in this population-based sample of 50- to 68-year-old adults. As Table 4 indicates, loneliness, depressive symptoms, perceived stress, and hostility were each significantly associated with SBP, whereas social support was unrelated to SBP.

Next, demographic and other covariates were held constant in linear regression models predicting SBP (see Table 5). Together, these variables accounted for between 12% and 16% of the variance in SBP, depending on the particular model being examined. Independent of age, BMI, alcohol consumption, smoking status, blood pressure medications, and demographic characteristics, SBP retained significant associations with loneliness, perceived stress, and hostility, accounting for an additional 3%, 2%, and 2% of the variance in SBP, respectively. In this set of models, depressive

symptoms no longer showed an association with SBP, and social support remained a nonsignificant predictor of SBP.

In the final model, all psychological predictors were added simultaneously with demographic and other covariates, thereby allowing us to examine whether covariation among the predictor variables obscured the independent impact of each predictor (see Table 5). Notably, the effect of loneliness on SBP was enhanced when the effects of depressive symptoms, stress, social support, and hostility were held constant. Similarly, the effect of perceived stress on SBP was greater when remaining predictors were held constant. Hostility failed to show a significant association with SBP independent of other psychosocial predictors. In contrast, net of the effects of remaining predictor variables, depressive symptoms were associated with lower SBP. Perceived stress and depressive symptoms were highly correlated, so to avoid collinearity, we examined effects when one or the other of these two variables was dropped from analyses. Neither perceived stress nor depressive symptoms retained a significant association with SBP when only one of the two was included in models with all other psychosocial predictor variables ($ps > .1$). Moreover, whether we dropped perceived stress or depressive symptoms from analyses, loneliness was the only psychosocial factor to retain a significant association with SBP.

Of importance, the addition of the Age \times Loneliness interaction term to the full model showed that loneliness and age interacted ($b = 0.7$, $SE = 0.3$, $p = .028$), such that SBP was higher by 0.7 mmHg per standard deviation of loneliness for each additional year of age (or conversely, an additional 0.7 mmHg per year for each standard deviation of loneliness). This interaction was plotted using a Web-based tool (Preacher, Curran, & Bauer, 2004; R Development Core Team, 2005) and is depicted in Figure 1. This result in a population-based sample replicates our prior research in which we found that, among older adults in a convenience sample, age was positively associated with SBP in lonely but not in nonlonely individuals (Cacioppo, Hawkley, Crawford, et al., 2002).

HR, RSA, and PEP. None of the correlational analyses showed significant associations between the psychosocial variables and HR or RSA ($ps > .18$). Loneliness and PEP tended to be inversely correlated, $r(181) = -.13$, $p = .09$, but this association did not withstand control for covariates ($p > .3$). Similarly, holding constant the demographic covariates did not reveal any significant

Table 3
Intercorrelations Between Psychosocial Predictor Variables

Variable	1	2	3	4	5
1. Loneliness (R-UCLA)	—				
2. Depressive symptoms (CES-D-ML) ^a	.57 (221)	—			
3. Perceived stress (PSS)	.48 (222)	.72 (220)	—		
4. Social support (ISEL)	-.58 (216)	-.41 (215)	-.44 (214)	—	
5. Hostility (CMHo)	.33 (210)	.38 (210)	.34 (209)	-.33 (207)	—

Note. *N*s are shown in parentheses. R-UCLA = Revised UCLA Loneliness Scale; CES-D-ML = Center for Epidemiologic Studies—Depression scale with loneliness item removed; PSS = Perceived Stress Scale; ISEL = Interpersonal Support Evaluation List; CMHo = Cook-Medley Hostility Scale.

^a Scores represent a sum of all items on the CES-D scale after removal of the loneliness item.

Table 4
Correlations Between Psychosocial Predictor Variables and Physiological Criteria

Variable	Loneliness (R-UCLA)	Depressive symptoms (CES-D-ML)	Perceived stress (PSS)	Social support (ISEL)	Hostility (CMHo)
SBP	.19** (219)	.15* (217)	.20** (217)	-.10 (212)	.23** (206)
HR	.05 (221)	.05 (219)	.08 (219)	.01 (214)	.05 (208)
RSA	-.01 (216)	-.01 (214)	-.04 (214)	-.08 (209)	-.10 (203)
PEP	-.13 (181)	-.11 (180)	-.01 (179)	.11 (177)	-.05 (172)
Urinary EPI	.17* (185)	.18* (183)	.18* (183)	-.10 (179)	.10 (178)
Urinary NEPI	.06 (183)	.13 [†] (182)	.11 (182)	-.05 (178)	.15* (177)
Urinary CORT	.07 (186)	-.004 (185)	.11 (184)	-.09 (181)	.15* (180)

Note. *N*s are shown in parentheses. R-UCLA = Revised UCLA Loneliness Scale; CES-D-ML = Center for Epidemiologic Studies—Depression scale with loneliness item removed; PSS = Perceived Stress Scale; ISEL = Interpersonal Support Evaluation List; CMHo = Cook–Medley Hostility Scale; SBP = systolic blood pressure; HR = heart rate; RSA = respiratory sinus arrhythmia; PEP = preejection period; EPI = epinephrine; NEPI = norepinephrine; CORT = cortisol.

[†] $p < .10$. * $p < .05$. ** $p < .01$.

associations between any of the psychosocial variables and HR or RSA.

Urinary Catecholamines

EPI. Correlational analyses (see Table 4) showed that loneliness, depressive symptoms, and perceived stress were associated with significantly higher levels of residualized urinary EPI ($ps < .05$). Female participants tended to have lower levels of urinary EPI (see Table 6) and, in conjunction with other control variables, explained 5% to 6% of the variance in urinary EPI, depending on the model. Holding gender, age, and other demographic variables constant, depressive symptoms and perceived stress continued to show significant associations with urinary EPI (see Table 6). The association between loneliness and urinary EPI approached significance when all covariates were held constant ($b = 14.1$, $p = .06$). In the full model, only perceived stress showed a tendency toward a significant independent association with urinary EPI ($b = 20.8$, $p = .08$; see Table 6). When depressive symptoms were dropped from the analysis (to avoid collinearity), the perceived stress effect attained statistical significance ($b = 22.6$, $p = .02$) and explained an additional 2% of the variance in urinary EPI. On the other hand, when perceived stress was dropped from the analysis, depressive symptoms no longer showed a significant association with urinary EPI ($p > .1$).

NEPI. Correlational analyses (shown in Table 4) showed a significant relationship between urinary NEPI and hostility and showed a tendency toward a positive association between urinary NEPI and depressive symptoms ($p = .09$). Among the covariates, gender and BMI were significant predictors of NEPI; female participants had lower levels of urinary NEPI, and higher BMI was associated with higher levels of urinary NEPI. In combination, the covariates explained 9% to 10% of the variance in urinary NEPI, depending on the model. Holding the covariates constant, NEPI was not associated with either the individual or the unique effects of the psychosocial variables ($ps > .13$; data not shown).

HPA Activity

Urinary cortisol. Correlational analyses showed that hostility was associated with elevated urinary cortisol (see Table 4), and

this relationship was retained in analyses in which all covariates were held constant (see Table 7). In combination, the covariates explained approximately 7% of the variance in urinary cortisol, and hostility individually explained an additional 2% of the variance. None of the other psychosocial variables was individually related to urinary cortisol, but when all were entered simultaneously into the regression equation, depressive symptoms showed an inverse association with urinary cortisol (see Table 7). However, when perceived stress was dropped from the analysis (to avoid collinearity), depressive symptoms no longer showed a significant association with urinary cortisol. Moreover, whether perceived stress or depressive symptoms were dropped from the analysis, hostility was the only psychosocial variable to retain a significant association with urinary cortisol.

Summary

Among the loneliness-related psychosocial variables examined, loneliness, perceived stress, and hostility exhibited significant individual associations with SBP independent of demographic and control variables. However, loneliness was the only psychosocial variable to exhibit a unique association with elevated SBP net of the remaining psychosocial variables (and the demographic and control variables). In addition, consistent with our primary hypothesis, a significant Loneliness \times Age interaction indicated that loneliness augmented age-related differences in SBP. Regarding other indices of physiological functioning, loneliness, perceived stress, and depressive symptoms exhibited significant individual associations with urinary EPI, and hostility exhibited a significant individual association with urinary cortisol. However, only perceived stress was uniquely associated with elevated levels of urinary EPI, and only hostility was uniquely associated with elevated levels of urinary cortisol, further supporting specific as opposed to general psychosocial stress effects. Indices of autonomic nervous system activity did not differ as a function of any of the psychosocial variables separately or in combination.

Discussion

In the past century, life expectancy in industrialized nations has nearly doubled and the major causes of morbidity and mortality

Table 5
Unstandardized Regression Coefficients Predicting Systolic Blood Pressure (SBP)

Variable	Loneliness model	Depressive symptoms model	Perceived stress model	Social support model	Hostility model	Unique effects model	Age × Loneliness model
Demographic and control variables: <i>b</i> (<i>SE</i>)							
Female	0.4 (2.8)	-0.6 (2.8)	-1.1 (2.8)	-1.0 (2.9)	-0.03 (2.9)	-0.5 (3.0)	-0.9 (3.0)
Ethnicity							
Black ^a	-0.3 (1.9)	-0.2 (2.0)	-0.3 (2.0)	0.2 (2.1)	-0.4 (2.0)	-0.6 (2.1)	-1.0 (2.0)
Hispanic ^a	-1.3 (2.0)	-1.6 (2.1)	-1.3 (2.0)	-1.1 (2.2)	-1.2 (2.1)	-1.0 (2.1)	-1.2 (2.1)
Age	0.4 (0.3)	0.4 (0.3)	0.4 (0.3)	0.5 (0.3)	0.3 (0.3)	0.2 (0.4)	0.2 (0.3) ^b
Married-cohabiting ^c	-1.9 (3.0)	-1.9 (3.1)	-2.7 (3.1)	-2.4 (3.2)	-3.4 (3.2)	-2.3 (3.2)	-2.9 (3.2)
Education	-1.2 (0.5)*	-1.1 (0.5)*	-1.1 (0.5)*	-1.1 (0.5)*	-0.9 (0.5)	-1.2 (0.5)*	-1.2 (0.5)*
Household income	-0.8 (1.7)	-1.4 (1.8)	-0.5 (1.8)	-1.4 (1.9)	-1.0 (1.8)	-0.6 (1.9)	-0.5 (1.8)
Cigarettes (packs-day)	9.3 (4.6)*	8.2 (4.7)	8.4 (4.7)	9.7 (5.0)	9.4 (4.8)*	10.0 (4.8)*	10.1 (4.7)*
Alcohol (drinks-day)	0.4 (0.7)	0.3 (0.7)	0.3 (0.7)	0.3 (0.7)	0.3 (0.7)	0.3 (0.7)	0.3 (0.7)
BMI	0.2 (0.2)	0.3 (0.2)	0.2 (0.2)	0.4 (0.2)	0.3 (0.2)	0.2 (0.2)	0.2 (0.2)
Vasoactive BP medication	4.9 (2.9)	5.6 (2.9)	4.7 (2.9)	5.6 (3.0)	5.5 (3.0)	4.6 (3.0)	4.1 (3.0)
Volume active BP medication	2.6 (4.1)	1.3 (4.1)	2.7 (4.1)	0.8 (4.2)	0.4 (4.2)	1.1 (4.1)	2.0 (4.1)
Complete SBP data	-4.9 (4.3)	-8.9 (4.6)	-7.1 (4.5)	-12.4 (5.1)*	-8.6 (6.0)	—	—
Standardized predictors: <i>b</i> (<i>SE</i>)							
Loneliness	3.2 (1.3)*					5.4 (1.9)**	4.9 (1.9)**
Depressive symptoms ^d		1.5 (1.5)				-5.1 (2.2)*	-4.5 (2.2)*
Perceived stress			3.0 (1.4)*			3.9 (2.0)*	4.0 (1.9)*
Social support				-1.1 (1.5)		3.2 (1.8)	2.9 (1.8)
Hostility					2.8 (1.4)*	2.1 (1.6)	1.9 (1.6)
Intercept (<i>SE</i>)	129.0 (28.8)	133.2 (30.1)	128.5 (29.6)	133.3 (30.5)	132.1 (30.6)	132.5 (31.2)	
<i>R</i> ² increment ^e	.025	.004	.020	.003	.017	.072	
<i>df</i>	1, 214	1, 212	1, 212	1, 208	1, 203	5, 192	
<i>F</i>	5.795*	1.003	4.688*	0.590	3.891*	3.110*	
Age × Loneliness (<i>SE</i>)							
Intercept (<i>SE</i>)							0.7 (0.3) ^{b,*}
<i>R</i> ² increment ^f							145.8 (20.1) ^b
<i>df</i>							.022
<i>F</i>							1, 192
							4.892*

Note. BMI = body mass index; BP = blood pressure; SBP = systolic blood pressure; CES-D = Center for Epidemiologic Studies—Depression scale. ^aThe reference group is Caucasian. ^bAge was mean-centered for this model. ^cThe reference group is divorced-separated, widowed, or never married. ^dA single loneliness item in the CES-D was removed before depressive symptom scores were calculated. ^eRelative to base model with demographic and control variables only. ^fRelative to full model with demographic, control, and all psychosocial variables. * $p < .05$. ** $p < .01$.

have changed from infectious to cardiovascular diseases. In the present research, we found that loneliness was positively associated with SBP in a population-based sample of middle-aged and older adults in a large metropolitan area, a finding that extends earlier work in a convenience sample showing age-related differences in SBP in lonely but not nonlonely older individuals (Cacioppo, Hawkley, Crawford, et al., 2002). The fact that loneliness predicted SBP in our cross-sectional study of middle-aged and older adults may be of clinical interest given that elevated SBP is a well-recognized (cross-sectional) risk factor for cardiovascular disease (Chobanian et al., 2003; Kannel, 1996). Whether loneliness causes elevated SBP is a topic for future research and requires longitudinal methods. Longitudinal research currently under way in our laboratory will provide data to address the causal role of loneliness and related psychosocial variables in influencing SBP.

Loneliness is a complex psychosocial phenomenon that incorporates feelings of dysphoria and stress, dissatisfaction with social support, and hostility toward others (Ernst & Cacioppo, 1999; Levin & Stokes, 1986; Shaver & Brennan, 1991). Separately, each of these affective and cognitive characteristics has been shown to contribute to individual differences in physiological functioning.

One aim of the present research was to examine whether the association between loneliness and SBP was specific to loneliness or was redundant with the associations between SBP and variables related to loneliness. In fact, the effect of loneliness on SBP was independent of the effects of depressive symptoms, perceived stress, social support, and hostility, indicating that loneliness is not redundant with these factors, but is a unique predictor and may make a unique contribution, through some means, to differences in SBP.

In the past, we have conjectured that appraisal and coping processes may contribute to loneliness differences in SBP (Cacioppo, Hawkley, Crawford, et al., 2002; Hawkley et al., 2003). Specifically, the threat appraisals and passive coping strategies that characterize lonely individuals (Cacioppo, Hawkley, Crawford, et al., 2002; Hawkley et al., 2003) have been associated with a primarily vascular response (Tomaka et al., 1993; Sherwood, Dolan, & Light, 1990) that we also observed in lonely young adults in the form of elevated levels of peripheral vascular resistance (Cacioppo, Hawkley, Crawford, et al., 2002; Hawkley et al., 2003). Holding constant any compensatory cardiovascular processes, increases in peripheral resistance result in increases in SBP.

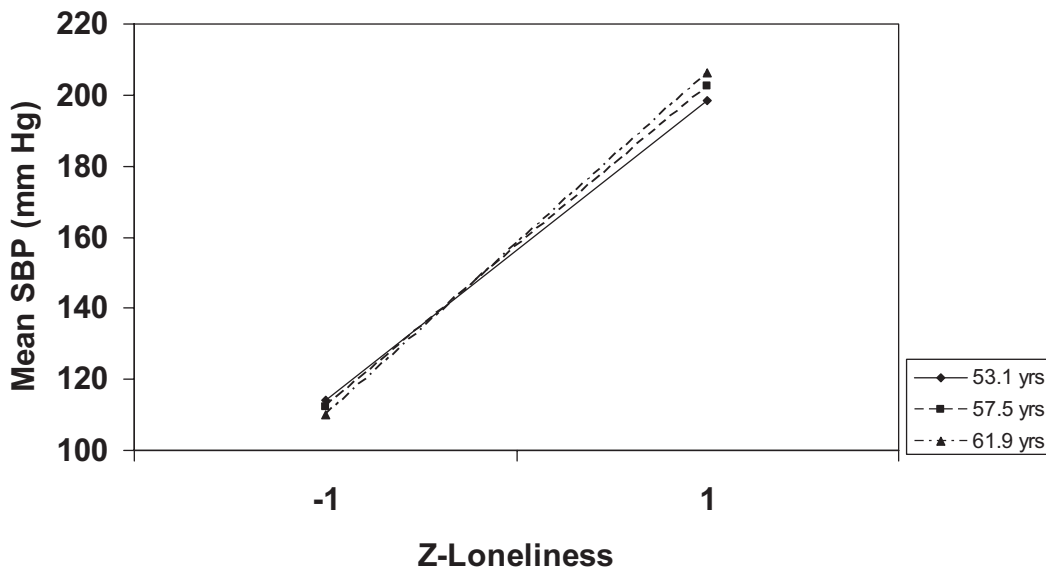


Figure 1. Systolic blood pressure (SBP) as a function of the interaction between loneliness and age. This figure was plotted from the following regression equation: $SBP = 0.2(\text{mean-centered age}) + 4.9(\text{standardized loneliness score}) + 0.7(\text{Standardized Loneliness Score} \times \text{Mean-Centered Age}) + 145.8$. yrs = years.

Although we did not observe loneliness differences in SBP in resilient young adults, we hypothesized that a vascular pattern of activation would be more likely to become evident in SBP increases in less physiologically resilient older adults. Our present

findings support this line of reasoning and show that the association between loneliness and SBP is exaggerated with increasing age.

A possible explanation that should be addressed for any association between loneliness and SBP is that lonely individuals may

Table 6
Unstandardized Regression Coefficients Predicting Urinary Epinephrine (EPI; Residualized)

Variable	Loneliness model	Depressive symptoms model	Perceived stress model	Social support model	Hostility model	Unique effects model
Demographic and control variables: <i>b</i> (<i>SE</i>)						
Female	-29.9 (15.2)*	-39.3 (15.1)**	-41.0 (15.2)**	-32.4 (15.4)*	-32.9 (16.0)*	-40.1 (17.3)*
Ethnicity						
Black ^a	15.8 (10.5)	15.2 (10.5)	16.5 (10.4)	18.2 (10.7) [†]	16.0 (10.9)	14.7 (11.3)
Hispanic ^a	-16.0 (11.2)	-17.3 (11.2)	-17.2 (11.3)	-16.2 (11.8)	-14.9 (11.8)	-16.7 (12.4)
Age	-2.2 (1.8)	-1.5 (1.8)	-2.0 (1.8)	-2.7 (1.8)	-3.0 (1.9)	-1.8 (2.0)
Married-cohabiting ^b	5.2 (16.9)	-0.1 (17.0)	-5.0 (17.2)	1.7 (17.3)	3.9 (18.0)	-6.2 (18.9)
Education	2.2 (3.1)	3.3 (3.0)	3.4 (3.0)	2.3 (3.0)	2.8 (3.2)	3.1 (3.2)
Household income	-4.9 (10.6)	-1.5 (10.7)	-0.8 (10.7)	-3.7 (10.8)	-8.3 (10.7)	3.9 (11.4)
BMI	0.7 (1.2)	0.3 (1.1)	.2 (1.2)	-0.05 (1.2)	0.08 (1.2)	0.1 (1.2)
Complete EPI data	19.7 (26.3)	29.5 (28.2)	20.3 (28.1)	18.7 (33.5)	6.1 (34.1)	—
Standardized predictors: <i>b</i> (<i>SE</i>)						
Loneliness	14.1 (7.4) [†]					5.8 (10.9)
Depressive symptoms ^c		21.6 (8.1)**				4.3 (12.6)
Perceived stress			22.9 (8.1)**			20.8 (11.8) [†]
Social support				-9.6 (7.6)		2.4 (10.1)
Hostility					8.0 (8.2)	-0.6 (9.1)
Intercept: (<i>SE</i>)	173.1 (176.7)	81.4 (183.3)	113.9 (178.3)	196.7 (181.0)	260.5 (184.9)	81.5 (197.2)
<i>R</i> ² increment ^d	.019	.038	.043	.009	.005	.056
<i>df</i>	1, 183	1, 181	1, 181	1, 177	1, 177	5, 168
<i>F</i>	3.593 [†]	7.112**	8.048**	1.595	0.939	1.945

Note. BMI = body mass index; CES-D = Center for Epidemiologic Studies—Depression scale.
^a The reference group is Caucasian. ^b The reference group is divorced-separated, widowed, or never married. ^c A single loneliness item in the CES-D was removed before depressive symptom scores were calculated. ^d Relative to base model with demographic and control variables only.
[†] *p* < .10. * *p* < .05. ** *p* < .01.

Table 7
Unstandardized Regression Coefficients Predicting Urinary Cortisol (CORT; Residualized)

Variable	Loneliness model	Depressive symptoms model	Perceived stress model	Social support model	Hostility model	Unique effects model
Demographic and control variables: <i>b</i> (<i>SE</i>)						
Female	-116.5 (112.7)	-122.9 (112.0)	-152.2 (113.2)	-112.5 (114.4)	-48.9 (116.8)	-45.2 (128.8)
Ethnicity						
Black ^a	-118.4 (77.1)*	-197.0 (77.7)*	-190.6 (77.4)*	-166.8 (79.5)*	-208.3 (78.1)**	-169.2 (84.2)*
Hispanic ^a	61.1 (83.3)	74.3 (84.4)	45.8 (85.1)	32.5 (88.1)	68.5 (85.5)	16.2 (93.0)
Age	-12.3 (13.1)	-12.6 (13.2)	-11.7 (13.3)	-15.1 (13.4)	-13.3 (13.2)	-26.5 (14.7) [†]
Married-cohabiting ^b	159.0 (125.0)	150.6 (126.9)	103.6 (129.9)	139.4 (129.1)	156.6 (130.5)	131.8 (142.5)
Education	-9.3 (20.6)	-7.2 (20.8)	-7.1 (20.7)	-11.1 (20.9)	0.8 (21.1)	-2.5 (21.8)
Household income	-51.3 (78.3)	-67.4 (80.2)	-34.0 (80.3)	-44.9 (80.6)	-52.4 (77.5)	-60.2 (85.1)
BMI	10.4 (8.5)	10.1 (8.4)	9.9 (8.5)	9.4 (8.5)	9.6 (8.5)	8.9 (8.9)
Complete CORT data	-4.0 (189.7)	10.9 (199.2)	63.4 (203.7)	98.6 (227.1)	121.2 (225.7)	—
Standardized predictors: <i>b</i> (<i>SE</i>)						
Loneliness	44.6 (55.0)					40.7 (81.6)
Depressive symptoms ^c		-0.2 (60.0)				-190.9 (92.5)*
Perceived stress			83.8 (59.3)			140.5 (86.1)
Social support				-49.8 (56.5)		17.4 (77.1)
Hostility					120.0 (57.6)*	162.5 (67.7)*
Intercept (<i>SE</i>)	1,154.7 (1,290.9)	1,327.0 (1,332.1)	938.0 (1,304.1)	1,203.9 (1,321.7)	885.8 (1,308.1)	1,916.1 (1,418.5)
<i>R</i> ² increment ^d	.003	.000	.011	.004	.023	.057
<i>df</i>	1, 184	1, 183	1, 182	1, 179	1, 179	5, 168
<i>F</i>	0.655	0.000	2.001	0.777	4.336*	2.028

Note. BMI = body mass index; CES-D = Center for Epidemiologic Studies—Depression scale.

^a The reference group is Caucasian. ^b The reference group is divorced-separated, widowed, or never married. ^c A single loneliness item in the CES-D was removed before depressive symptom scores were calculated. ^d Relative to base model with demographic and control variables only.

[†] $p < .1$. * $p < .05$. ** $p < .01$.

be less likely to utilize medical services or to use blood pressure medication. In our investigation of health behaviors in this sample of middle-aged and older adults (Cacioppo & Hawkey, 2005), we determined that the utilization of medical services (e.g., physician visits) did not differ as a function of loneliness. In the present study, the use of blood pressure medication did not differ as a function of loneliness. Therefore, the loneliness-related differences in SBP observed in the current study cannot be explained by poorer access to and use of medical services.

The magnitude of the association between loneliness and blood pressure was sizable: When we held constant age and all other demographic and psychosocial covariates, an increase of 1 standard deviation in loneliness (10 units on a 60-unit scale) was associated with an SBP difference of more than 5 mm Hg, an effect roughly equivalent to 5 years of typical age-related increases in SBP during the adult years (20–80 years; Izzo, Levy, & Black, 2000; Staessen et al., 2003). Thus, across the entire range of scores on the R-UCLA Loneliness scale, individuals scoring in the top third of the scale would be predicted to have SBP levels 10 to 30 mm higher than those scoring in the bottom third of the scale. This effect size is reminiscent of the 20 mm Hg difference in SBP that doubled the risk of mortality from stroke, ischemic heart disease, or other vascular disease in a prospective study of 40- to 69-year-old individuals (Lewington, Clarke, Qizilbash, Peto, & Collins, 2002). Conversely, SBP is reduced by 5 to 20 mm Hg with a 10-kg weight loss, and by 4 to 9 mm Hg with regular physical activity (Chobanian et al., 2003). By these standards, improvements in a sense of social connectedness may have clinical benefits comparable to, if not greater than, lifestyle modifications. Longitudinal research is needed to test this possibility, however.

Given our prior observations (Cacioppo, Hawkey, Crawford, et al., 2002), we included a test of the Age \times Loneliness effect on SBP. This test revealed a significant interaction between loneliness and age (0.7 mm Hg/year/standard deviation of loneliness), indicating that the loneliness effect was stronger among older individuals. These effects support the notion that loneliness-related differences in blood pressure may develop gradually and may contribute to broad-based morbidity and mortality. A gradual increase in SBP could be attributable to the gradual cumulative cardiovascular effects of enduring loneliness across the life span and/or an increasing vulnerability to the cardiovascular consequences of loneliness in an already aging organism, among other possibilities. The causal role of loneliness awaits longitudinal analyses.

An additional aim of the present research was to examine whether the association between loneliness and SBP reflects a specific physiological stress response, or whether loneliness is associated with a general stress response evident in other indices of physiological functioning. Using overnight urinary EPI levels as an indicator of SNS functioning, we found that evidence supported specificity in associations between psychosocial stress and physiological processes. Higher levels of urinary EPI were uniquely associated with perceived stress and were not independently associated with loneliness or any other psychosocial stress factor. The facts that perceived stress was associated with higher urinary EPI excretion rates, and urinary EPI excretion has been found to predict mortality (Reuben et al., 2000), are consistent with the notion that perceived stress may contribute to increased morbidity and mortality.

Differential associations between psychosocial risk factors and HPA activity provided additional evidence supporting specificity in pathways linking psychosocial stress and physiological functioning. Higher levels of urinary cortisol were uniquely associated with hostility and were not independently associated with loneliness or any other psychosocial stress factor. An association between hostility and cortisol excretion was also demonstrated by Pope and Smith (1991), who found that men who were high in hostility excreted nearly double the cortisol excreted by men who were low in hostility during the day. The present study replicates this work using a population-based sample of middle-aged and older adults. Glucocorticoids, such as cortisol, are essential to mobilize bodily resources on need-based demand, but chronically elevated levels of circulating cortisol are thought to contribute to immune suppression, decrements in cognitive performance (e.g., memory), abdominal obesity (a risk factor for diabetes and cardiovascular disease, among others), and a variety of other adverse sequelae (Dallman et al., 2003; Seeman, McEwen, Singer, Albert, & Rowe, 1997; Tsigos & Chrousos, 2002). Our results support the idea that hostility is a risk factor for poor health and that increased HPA activity may explain some of the health effects.

We also examined whether loneliness and related psychosocial variables were associated with tonic autonomic control of the heart and found no significant associations with HR, PEP, or RSA. Whether loneliness, perceived stress, depressive symptoms, hostility, and/or social support contribute to individual differences in autonomic reactivity to psychological stressors will have to be addressed in future research.

In summary, the current study of a population-based sample of men and women 50 to 68 years of age indicates that elevated blood pressure may be one mechanism through which loneliness is related to morbidity and mortality. Specifically, elevated blood pressure may mark the onset and/or progression of hypertension, and hypertension is a major risk factor for cardiovascular disease, the primary cause of morbidity and mortality in industrialized nations. Moreover, loneliness may augment age-related increases in blood pressure, thereby further increasing risk for hypertension in aging adults whose physiological resilience is declining. Hypertension has diverse determinants, and additional research is needed to examine the mechanism(s) by which loneliness contributes to elevated blood pressure. Individual differences in endothelial function, renal function, blood lipids, and inflammation, for example, represent potential pathways by which loneliness may influence blood pressure. This study of middle-aged and older adults did not support a role for loneliness in influencing HPA functioning as indexed using a cumulative measure of overnight urinary cortisol. Rather, hostility was unique in its association with altered (i.e., exaggerated) HPA activity. In addition, loneliness had only an indirect effect on sympathoadrenomedullary activity through stress perceptions that were associated with elevated overnight urinary EPI. The unique patterns of association between the cluster of loneliness-related psychosocial risk factors and measures of physiological activity reinforce the value of a nuanced approach to physiological stress responses. Indeed, these data support our claim that it is precisely because individual psychosocial factors have different psychological and behavioral effects that physiological mechanisms and outcomes differ.

As has been noted throughout, this study is limited by its correlational nature; causal statements about the role of loneliness

(and its constellation of related psychosocial variables) await the results of longitudinal research. In addition, missing data are a feature of population-based studies of this kind, and although there were no systematic differences between participants for whom there were or were not missing data, we cannot rule out that participants with missing data might have exhibited a different pattern of associations between psychosocial and physiological variables. Finally, although age and age interaction effects are sometimes reducible to cohort effects (e.g., in convenience samples), our randomly selected population-based design enhances the generalizability of the observed Loneliness \times Age association with SBP. In light of these findings, demographic changes in the United States portend health crises. Not only is the U.S. population aging but household size is decreasing, the number of people living alone is increasing, and geographic mobility continues to separate people from the love and support of caring friends and family members (Hobbs & Stoops, 2002). Under these circumstances, risk of loneliness increases, and along with it, so does risk of morbidity and mortality. For instance, in their review of the relevant literature, Rozanski et al. (1999) reported that among initially healthy populations, those with smaller or less diverse social networks, less frequent social interactions, or fewer people living in the household had significantly increased risk for cardiac and all-cause mortality 2 to 15 years later. Given the rapidly aging U.S. population, the health risks associated with social isolation and loneliness will place a growing proportion of these physiologically vulnerable individuals at increased risk for poor cardiovascular health.

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