Social isolation, loneliness, and all-cause mortality in older men and women

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Both social isolation and loneliness are associated with increased mortality, but it is uncertain whether their effects are independent or whether loneliness represents the emotional pathway through which social isolation impairs health. We therefore assessed the extent to which the association between social isolation and mortality is mediated by loneliness. We assessed social isolation in terms of contact with family and friends and participation in civic organizations in 6,500 men and women aged 52 and older who took part in the English Longitudinal Study of Ageing in 2004-2005. A standard guestionnaire measure of loneliness was administered also. We monitored all-cause mortality up to March 2012 (mean follow-up 7.25 y) and analyzed results using Cox proportional hazards regression. We found that mortality was higher among more socially isolated and more lonely participants. However, after adjusting statistically for demographic factors and baseline health, social isolation remained significantly associated with mortality (hazard ratio 1.26, 95% confidence interval, 1.08-1.48 for the top quintile of isolation), but loneliness did not (hazard ratio 0.92, 95% confidence interval, 0.78-1.09). The association of social isolation with mortality was unchanged when loneliness was included in the model. Both social isolation and loneliness were associated with increased mortality. However, the effect of loneliness was not independent of demographic characteristics or health problems and did not contribute to the risk associated with social isolation. Although both isolation and loneliness impair quality of life and well-being, efforts to reduce isolation are likely to be more relevant to mortality.

Social relationships are central to human well-being and are critically involved in the maintenance of health (1, 2). Social isolation is an objective and quantifiable reflection of reduced social network size and paucity of social contact. It is a particular problem at older ages, when decreasing economic resources, mobility impairment, and the death of contemporaries conspire to limit social contacts. Socially isolated individuals are at increased risk for the development of cardiovascular disease (3), infectious illness (4), cognitive deterioration (5), and mortality (6–9). Social isolation also has been associated with elevated blood pressure, C-reactive protein, and fibrinogen (10, 11) and with heightened inflammatory and metabolic responses to stress (12, 13).

Loneliness often is regarded as the psychological embodiment of social isolation, reflecting the individual's experienced dissatisfaction with the frequency and closeness of their social contacts or the discrepancy between the relationships they have and the relationships they would like to have (14). Loneliness itself has been linked with increased risk of cardiovascular disease and mortality (15–18), elevated blood pressure and cortisol (19–21), heightened inflammatory responses to stress (22, 23), and modifications in transcriptional pathways linked with glucocorticoid and inflammatory processes (24).

A key scientific question is whether social isolation and loneliness are two independent processes, each contributing to health risk, or whether the emotional state of loneliness, through its biological concomitants, provides a mechanism through which social isolation affects health. Previous studies have yielded mixed results (18, 25–27). The issue is important because its answer will help identify the most effective levers for change and the best approaches for support of older people. The purpose of our study was to investigate the associations of social isolation and loneliness with mortality in a representative national sample of older men and women and to test whether loneliness is partly responsible for the association between social isolation and mortality.

Results

We carried out these analyses on 6,500 men and women who participated in wave 2 of the English Longitudinal Study of Ageing (ELSA) in 2004–2005 (28), tracking mortality until March 2012. We defined social isolation and loneliness as having a score within the top quintile, so for the purposes of Cox regression modeling we compared participants with high (18.5%) and low/ average (81.5%) scores on our social isolation index and high (18.1%) and low/average (81.9%) loneliness scores on the short form of the Revised University of California, Los Angeles (UCLA) loneliness scale (29). The characteristics of the high and low/average social isolation and high and low/average loneliness groups are summarized in Table 1. There were no sex differences in social isolation, but isolated individuals were more likely to be older and unmarried with limited education and lower wealth. Social isolation also was associated with limiting longstanding illnesses such as chronic lung disease, arthritis, impaired mobility, and depressive symptoms. Loneliness was more common in women and was associated with older age, less education, and lower wealth and marital status in the same way as social isolation. It was associated with a greater range of health conditions than social isolation, including coronary heart disease (CHD), stroke, and clinical depression, although the prevalence of these conditions was low. Loneliness ratings averaged 4.06 ± 1.47 , similar to levels described in comparable studies in the United States (26). Social isolation and loneliness were positively correlated ($\rho = 0.10, P < 0.001$).

We found that 918 (14.1%) of the 6,500 participants in ELSA had died by the census date, with a higher rate among men than women (16.3 vs. 12.3%, P < 0.001). Both social isolation and loneliness were associated with all-cause mortality; the absolute proportions of deaths were 21.9 vs. 12.3% in the high and low/ average isolation groups and 19.2 vs. 13.0% in the high and low/ average loneliness groups, respectively.

Cox proportional hazard analyses showed that, after adjustment for age and sex, the hazards ratio (HR) for mortality was 1.50 [95% confidence interval (CI), 1.30–1.73, P < 0.001] in the high social isolation group (Table 2). Adjustment for demographic

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Table 1. Social isolation, loneliness, and risk factors

| | Social isolation | | | Loneliness | | |
|-------------------------------------|--------------------------------|---------------------------------|---------|--------------------------------|--------------------------------|---------|
| Patient characteristics | Low/average (n = 5,269) (%) | High (<i>n</i> = 1,231) (%) | P value | Low/average (n = 5,325) (%) | High (<i>n</i> =1,175) (%) | P value |
| Sex | | | | | | |
| Male | 2,378 (45.1) | 575 (46.7) | 0.32 | 2,522 (47.4) | 431 (36.7) | <0.001 |
| Female | 2,891 (54.9) | 656 (53.3) | | 2,803 (52.6) | 744 (63.3) | |
| Age (y) | | | | | | |
| <60 | 1,709 (32.4) | 353 (28.7) | <0.001 | 1,719 (32.3) | 343 (29.2) | <0.001 |
| 60–69 | 1,888 (35.8) | 359 (29.2) | | 1,904 (35.8) | 343 (29.2) | |
| 70–79 | 1,219 (23.1) | 325 (26.4) | | 1,248 (23.4) | 296 (25.2) | |
| 80+ | 453 (8.6) | 194 (15.8) | | 454 (8.5) | 193 (16.4) | |
| Education | | | | | | |
| No qualifications | 1,675 (31.8) | 572 (46.5) | <0.001 | 1,733 (32.5) | 514 (43.7) | <0.001 |
| Intermediate | 2,099 (39.8) | 435 (35.3) | | 2,101 (39.5) | 433 (36.9) | |
| Higher education | 1,495 (28.4) | 224 (18.2) | | 1,491 (28.0) | 228 (19.4) | |
| Ethnicity (White) | 5,202 (98.7) | 1,217 (98.9) | 0.78 | 5,266 (98.9) | 1,153 (98.1) | 0.041 |
| Wealth guintile | | | | | | |
| 1 (lowest) | 720 (13.7) | 382 (31.0) | <0.001 | 793 (14.9) | 309 (26.3) | <0.001 |
| 2 | 990 (18.8) | 270 (21.9) | | 984 (18.5) | 276 (23.5) | |
| 3 | 1,101 (20.9) | 223 (18.1) | | 1,095 (20.6) | 229 (19.5) | |
| 4 | 1,208 (22.9) | 183 (14.9) | | 1,191 (22.4) | 200 (17.0) | |
| 5 (highest) | 1,250 (23.7) | 173 (14.1) | | 1,262 (23.7) | 161 (13.7) | |
| Married | 4,089 (77.6) | 388 (31.5) | <0.001 | 3,971 (74.6) | 506 (43.1) | <0.001 |
| Limiting long-standing illness | 1,629 (30.9) | 485 (39.4) | <0.001 | 1,540 (28.9) | 574 (48.9) | <0.001 |
| Cancer | 168 (3.2) | 36 (2.9) | 0.72 | 171 (3.2) | 33 (2.8) | 0.52 |
| Diabetes | 332 (6.3) | 89 (7.2) | 0.25 | 332 (6.2) | 89 (7.6) | 0.10 |
| CHD | 193 (3.7) | 43 (3.5) | 0.87 | 176 (3.3) | 60 (5.1) | 0.004 |
| Chronic lung disease | 65 (1.2) | 34 (2.8) | <0.001 | 71 (1.3) | 28 (2.4) | 0.012 |
| Stroke | 134 (2.5) | 43 (3.5) | 0.079 | 117 (2.2) | 60 (5.1) | <0.001 |
| Arthritis | 1,778 (33.7) | 477 (38.7) | 0.001 | 1,714 (32.3) | 541 (46.0) | <0.001 |
| Mobility impairment | 2,940 (55.8) | 769 (62.5) | <0.001 | 2871(53.9) | 838 (71.3) | <0.001 |
| Clinical depression | 77 (1.5) | 21(1.7) | 0.52 | 59 (1.1) | 39 (3.3) | <0.001 |
| Depression symptoms above threshold | 883 (16.8) | 338 (27.5) | <0.001 | 690 (13.0) | 531 (45.2) | <0.001 |

factors including marital status reduced the strength of this association by around 36% (model 2), with a further reduction of 12% when baseline health status and depression were taken into account (model 3). Nevertheless, the HR remained highly significant (1.26, 95% CI, 1.07–1.48, P = 0.005). This result indicates that the mortality risk of social isolation is caused partly by social disadvantage or poor health, but much of the association remains unexplained. Adding loneliness to the model did not reduce the HR for social isolation, and there was no interaction between social isolation and loneliness. In the fully adjusted model, other significant predictors of mortality were being older, male, less wealthy, having a limiting longstanding illness, cancer, or CHD at baseline, mobility impairment, and depressive symptoms (Table S1 shows the full regression model). We tested sex differences in these patterns by adding the two-way social isolation by sex interaction (HR 0.85, 95% C.I. 0.64–1.14, P = 0.27), but the effect was not significant.

The age- and sex-adjusted HR for loneliness was significant (1.26, 95% CI, 1.08–1.46, P = 0.003) but was reduced to nonsignificance when demographic factors were included (model 2, Table 3). The association was attenuated further after baseline health and mobility were included in the model (HR 0.92, 95% CI, 0.78–1.09, P = 0.34), suggesting that social disadvantage and concurrent health problems largely account for the relationship between loneliness and mortality. There was no significant interaction between loneliness and sex (HR 0.93, 95% CI, 0.68–1.26, P = 0.63).

We carried out two sensitivity analyses. The first tested the reverse causality hypothesis, that serious illness presaging early death had preceded the measurement of social isolation and loneliness, by repeating the analysis after excluding all fatalities

| Table 2. | Association | between | social | isolation | and | mortality |
|----------|-------------|---------|--------|-----------|-----|-----------|
| | | | | | | |

| | | Social isolation | | |
|-------|---|------------------|---------|--|
| Model | Covariates | HR (95% C.I.) | P value | |
| 1 | Isolation + age + sex | 1.50 (1.30–1.73) | <0.001 | |
| 2 | Isolation + age + sex + demographic factors* | 1.32 (1.12–1.54) | <0.001 | |
| 3 | Isolation + age + sex + demographic factors* + health indicators [†] | 1.26 (1.07–1.48) | 0.005 | |
| 4 | Model 3 + Ioneliness | 1.26 (1.08–1.48) | 0.004 | |

*Demographic factors are wealth, education, marital status, and ethnicity.

[†]Health indicator are limiting long-standing illness, mobility impairment, cancer, diabetes, CHD, chronic lung disease, arthritis, stroke, diagnosed depression, and CES-D rating.

Table 3. Association between loneliness and mortality

| | | Lonelines | s |
|-------|---|------------------|---------|
| Model | Covariates | HR (95% C.I.) | P value |
| 1 | Loneliness + age + sex | 1.26 (1.08–1.46) | 0.003 |
| 2 | Loneliness + Age + sex + demographic factors* | 1.14 (0.98–1.34) | 0.095 |
| 3 | Loneliness + age + sex + demographic factors* + health indicators ^{$+$} | 0.92 (0.78–1.09) | 0.34 |

*Demographic factors are wealth, education, marital status, and ethnicity.

[†]Health indicators are limiting long-standing illness, mobility impairment, cancer, diabetes, CHD, chronic lung disease, arthritis, stroke, diagnosed depression, and CES-D rating.

in the first 24 mo after baseline. The results are comparable to those in the main analysis (Table S2). The HR for social isolation remained significant in the fully adjusted model (1.33, 95% CI, 1.11–1.58, P = 0.002).

Our second sensitivity analysis tested social isolation and loneliness as continuous variables, instead of the categories used in the Cox regression. The results were unchanged from those in the categorical analyses, with an adjusted odds ratio of death of 1.26 (95% CI 1.13–1.41, P < 0.001) for every unit increase in social isolation and no significant relationship with loneliness (odds ratio 1.00, 95% CI 0.94–1.06, see Table S3).

Discussion

We found that both social isolation and loneliness predicted mortality over 7 y of follow-up in a national sample of older men and women. The association between social isolation and mortality remained strong after demographic factors and baseline health and mobility had been taken into account in multivariable models, but the association between loneliness and mortality was largely accounted for by baseline mental and physical health. There were no significant sex differences in these findings.

Our results indicate that loneliness did not affect the independent association between social isolation and mortality, and this conclusion was unchanged when deaths during the first 2 y after baseline were excluded. This finding suggests that the subjective experience of loneliness—often thought to be the psychological manifestation of social isolation—is not the primary mechanism explaining the association between social isolation and mortality in this study.

The levels of loneliness in this sample were comparable with those reported in the Health and Retirement Study (HRS) in the United States using the same measure (26). As in other older samples, loneliness tended to be higher in women and in those from more disadvantaged circumstances (30). It is notable that loneliness was more strongly related to baseline poor health than was social isolation, particularly with respect to arthritis, mobility impairment, and depression (Table 1). Our finding that loneliness no longer was associated with mortality after covariates had been taken into account likely reflects its relationship with baseline health. The result is consistent with previous studies. In the HRS, loneliness predicted all-cause mortality over a 6-y period independently of demographic factors and health behaviors, but associations no longer were significant after baseline health, functional limitations, and depressive symptoms were taken into account (26). Similarly in a sample of older people in Japan, the association of loneliness with mortality was mediated through linkage with chronic disease and functional impairment (31). These results do not imply that loneliness is not important but rather indicate that the experience of loneliness may be characteristic of people who already have major health and mobility problems. They also suggest that the health implications of loneliness may be overestimated if studies do not take account of the strength of objective social connections (17, 18).

If emotional processes indexed by loneliness do not explain the adverse effects of social isolation on survival, alternative mechanisms need to be investigated. Lifestyle may be relevant (11), including habitual health-risk behaviors such as smoking, inactivity, and unhealthy diets and health-protective behaviors such as adherence to medical recommendations, all of which may be vulnerable to lack of social support. In addition, people who live alone or lack social contacts may be at increased risk of death if acute symptoms develop, because there is less of a network of confidantes to prompt medical attention (9). Social contact itself also may have specific biological consequences that are important for health maintenance (10-13).

It should be noted that our analysis of continuously distributed social isolation and loneliness ratings produced findings similar to those involving high isolation and loneliness groups. This similarity suggests that the associations reflect variations in risk across the full spectrum of social connectedness rather than a phenomenon limited to individuals who are extremely isolated or lonely. Social isolation is a growing problem among middleaged and older people. In 2011, people living alone comprised 28% of all households in the United States, compared with 17% in 1970 (32). The proportion of Americans who said they had no one to talk to about important matters increased from 10% in 1985 to 25% in 2004 (33), and in the 2010 European Social Survey, 27% of respondents aged 50 y and over met friends, relatives, or colleagues once a month or less (34). Between 1996 and 2012, the proportion of people aged 45-64 y who lived alone in England and Wales rose by 53% (35).

One concern in all observational studies is reverse causality; i.e., that social isolation may be more common in people who are critically ill, and that the mortality is higher because of the greater proportion of illness, not because of social isolation. This possibility cannot be ruled out completely, but we repeated the analysis excluding deaths within 24 mo of baseline, and the results were very similar results to those for the full cohort, suggesting that existing terminal illness is not the primary explanation. However, it is possible that some other unmeasured factors were responsible for the findings.

The strengths of this analysis include the use of a large representative population cohort in which it was possible to control for multiple health and demographic indicators. We also were able to construct a comprehensive social isolation index that included contacts with friends, relatives, and family as well as civic participation. The primary limitation is that it is not possible to draw causal conclusions from an observational study of this kind. Although the response rate was high, nonresponders in wave 2 of ELSA tended to be older and less well educated (28). We gave equal weight to different aspects of social contact in these analyses, but some social relationships may be more important to future health than others.

The findings of this study confirm that social isolation is associated with higher mortality in older men and women but indicate that this effect is independent of the emotional experience of loneliness. Reducing both social isolation and loneliness are important for quality of life and well-being, but efforts to reduce isolation would be likely to have greater benefits in terms of mortality.

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Materials and Methods

Participants. The data analyzed in this study are from a population-based cohort study involving 6.500 men and women who took part in wave 2 of the ELSA in 2004–2005. The ELSA is a longitudinal panel study of men and women aged 50 y or more living in England that started in 2002, with the sample being drawn from households that previously had participated in the Health Survey for England in 1998, 1999, and 2001 (28). Comparisons of the sociodemographic characteristics of participants with the national census show that at baseline the sample was representative of the English population. Participants are reassessed every 2 y. Social isolation was measured in wave 1, but loneliness assessments were introduced in wave 2, so wave 2 was used as the baseline for these analyses. The response rate in wave 2 was 81.5% of eligible participants. Ethical approval for ELSA was given by the National Research Ethics Service. All-cause mortality up to March 2012 was supplied by the National Health Service central data registry for all participants who consented to mortality follow-up (96.5%). The mean follow-up period was 7.25 y ± 2.8 mo.

Measures of Social Isolation and Loneliness. We created an index of social isolation by assigning one point if the respondent was unmarried/not cohabiting, had less than monthly contact (including face-to-face, telephone, or written/e-mail contact) with each of children, other family members, and friends, and if they did not participate in organizations such as social clubs or residents groups, religious groups, or committees (11). Scores ranged from 0 to 5, with higher scores indicating greater social isolation. We measured loneliness with the three-item short form of the Revised UCLA loneliness scale (29). An example of an item is "How often do you feel you lack companionship?" with response options of hardly ever or never, some of the time, and often. Ratings were summed to produce a loneliness score ranging from 3 to 9, with a higher score indicating greater loneliness. Both social isolation and loneliness were positively skewed, so for the purpose of Cox regression modeling we defined the top quintile (≥2 for social isolation and ≥6 for loneliness) as isolated or lonely respectively. Allowing for ties, this resulted in 1,231 isolated and 5,269 nonisolated respondents and 1,175 lonely and 5,325 nonlonely participants. In sensitivity analyses, we used continuous scores of social isolation and loneliness to check whether associations were linked to extreme scores.

Other Measures. We indexed socioeconomic status by total household wealth, including financial wealth, the value of any home and other property, the value of business assets, and physical wealth such as artwork and jewelry, net of debt. Wealth is a robust indicator of socioeconomic circumstances and standard of living in ELSA (36) and was divided into age-related quintiles for the purposes of analysis. Educational attainment was divided into three categories: no formal qualifications, intermediate (equivalent to junior high school and high school), and higher education (college education). Marital status was classified into married or equivalent versus other (never married, divorced, separated, widowed). Ethnicity was categorized as white or other. We assessed general health by asking participants if they suffered from one or more long-standing illnesses and if these illnesses limited daily activities. The two questions were combined to form a dichotomous variable, indicating whether participants suffered from any limiting long-standing

- 1. House JS, Landis KR, Umberson D (1988) Social relationships and health. *Science* 241(4865):540–545.
- Holt-Lunstad J, Smith TB, Layton JB (2010) Social relationships and mortality risk: A meta-analytic review. PLoS Med 7(7):e1000316.
- Barth J, Schneider S, von Känel R (2010) Lack of social support in the etiology and the prognosis of coronary heart disease: A systematic review and meta-analysis. *Psycho*som Med 72(3):229–238.
- Cohen S, Doyle WJ, Skoner DP, Rabin BS, Gwaltney JM, Jr. (1997) Social ties and susceptibility to the common cold. JAMA 277(24):1940–1944.
- Bassuk SS, Glass TA, Berkman LF (1999) Social disengagement and incident cognitive decline in community-dwelling elderly persons. Ann Intern Med 131(3):165–173.
- Eng PM, Rimm EB, Fitzmaurice G, Kawachi I (2002) Social ties and change in social ties in relation to subsequent total and cause-specific mortality and coronary heart disease incidence in men. Am J Epidemiol 155(8):700–709.
- Heffner KL, Waring ME, Roberts MB, Eaton CB, Gramling R (2011) Social isolation, C-reactive protein, and coronary heart disease mortality among community-dwelling adults. Soc Sci Med 72(9):1482–1488.
- Kaplan GA, et al. (1988) Social connections and mortality from all causes and from cardiovascular disease: Prospective evidence from eastern Finland. Am J Epidemiol 128(2):370–380.
- Udell JA, et al. (2012) REduction of Atherothrombosis for Continued Health (REACH) Registry Investigators (2012) Living alone and cardiovascular risk in outpatients at risk of or with atherothrombosis. *Arch Intern Med* 172(14):1086–1095.

illness. We also asked respondents whether they had a physician diagnosis of CHD, cancer, stroke, diabetes, arthritis, or chronic lung disease. Because depression is a risk factor for mortality from common serious illness (37-39) and also is associated with social isolation and loneliness, it was included as an additional covariate. We recorded physician diagnoses of depressive illness, and depressive symptoms were measured using the eight-item Centre for Epidemiologic Studies Depression Scale (CES-D), as used extensively in ELSA, the HRS, and other population cohorts (40). The item on loneliness was omitted from the CES-D to avoid direct overlap with the loneliness scale (41); however, the same results emerged when this item was included. A binary variable was created with respondents reporting three or more symptoms being classified as depressed. Mobility impairment was also included as a covariate, because it might increase social isolation and loneliness. Respondents were asked whether they had difficulties with 10 common leg and arm functions (e.g., walking 100 yards, lifting more than 10 pounds). We analyzed mobility impairment as a binary variable (present, absent). Similar results emerged when depressive symptoms and the number of impairments were included as continuous variables.

Statistical Analysis. The characteristics of participants low/average and high in social isolation and low/average and high in loneliness were compared using ² tests. We used Cox proportional hazards regression models to estimate the HRs of all-cause mortality and 95% CIs associated with social isolation, using the low/average isolation group as the reference category. Survival time was measured in months from the date of interview to the date of death or to follow-up in March 2012. We fitted four models. Model 1 was adjusted for age and sex. We added demographic factors (wealth, education, marital status, and ethnicity) to model 2. In model 3, we added health indicators at baseline, including limiting longstanding illness, cancer, CHD, stroke, diabetes, arthritis, and chronic lung disease, indicators of depression (specifically CES-D score and diagnosis of depression), and baseline mobility impairment. Loneliness was added to model 4. We also tested whether the association of social isolation with mortality differed in men and women by adding appropriate interaction terms into the models, but the interactions were not significant so results stratified by sex are not presented. Similar modeling was carried out for loneliness, using the low/average loneliness group as the reference category.

We carried out two sensitivity analyses. First, we repeated the Cox regression analyses after excluding deaths that occurred within 24 mo of baseline, to guard against the possibility that associations were caused by individuals having become isolated or lonely as a consequence of illness. Second, we tested whether similar results would be observed if social isolation and loneliness were modeled as continuous variables, carrying out logistic regression on mortality on the census date.

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- Loucks EB, Berkman LF, Gruenewald TL, Seeman TE (2006) Relation of social integration to inflammatory marker concentrations in men and women 70 to 79 years. *Am J Cardiol* 97(7):1010–1016.
- Shankar A, McMunn A, Banks J, Steptoe A (2011) Loneliness, social isolation, and behavioral and biological health indicators in older adults. *Health Psychol* 30(4): 377–385.
- Grant N, Hamer M, Steptoe A (2009) Social isolation and stress-related cardiovascular, lipid, and cortisol responses. Ann Behav Med 37(1):29–37.
- Uchino BN (2006) Social support and health: A review of physiological processes potentially underlying links to disease outcomes. J Behav Med 29(4):377–387.
- Peplau LA, Perlman D (1982) Perspectives on loneliness. Loneliness: A Sourcebook of Current Theory, Research and Practice, eds Peplau LA, Perlman D (John Wiley, New York), pp 1–17.
- Patterson AC, Veenstra G (2010) Loneliness and risk of mortality: A longitudinal investigation in Alameda County, California. Soc Sci Med 71(1):181–186.
- Shiovitz-Ezra S, Ayalon L (2010) Situational versus chronic loneliness as risk factors for all-cause mortality. Int Psychogeriatr 22(3):455–462.
- Thurston RC, Kubzansky LD (2009) Women, loneliness, and incident coronary heart disease. Psychosom Med 71(8):836–842.
- Perissinotto CM, Stijacic Cenzer I, Covinsky KE (2012) Loneliness in older persons: A predictor of functional decline and death. Arch Intern Med 172(14):1078–1083.
- Cacioppo JT, et al. (2000) Lonely traits and concomitant physiological processes: The MacArthur social neuroscience studies. Int J Psychophysiol 35(2-3):143–154.

- Doane LD, Adam EK (2010) Loneliness and cortisol: Momentary, day-to-day, and trait associations. Psychoneuroendocrinology 35(3):430–441.
- Hawkley LC, Thisted RA, Masi CM, Cacioppo JT (2010) Loneliness predicts increased blood pressure: 5-year cross-lagged analyses in middle-aged and older adults. *Psychol Aging* 25(1):132–141.
- Steptoe A, Owen N, Kunz-Ebrecht SR, Brydon L (2004) Loneliness and neuroendocrine, cardiovascular, and inflammatory stress responses in middle-aged men and women. *Psychoneuroendocrinology* 29(5):593–611.
- Hackett RA, Hamer M, Endrighi R, Brydon L, Steptoe A (2012) Loneliness and stressrelated inflammatory and neuroendocrine responses in older men and women. *Psychoneuroendocrinology* 37(11):1801–1809.
- 24. Cole SW, et al. (2007) Social regulation of gene expression in human leukocytes. Genome Biol 8(9):R189.
- Holwerda TJ, et al. (2012) Increased risk of mortality associated with social isolation in older men: Only when feeling lonely? Results from the Amsterdam Study of the Elderly (AMSTEL). *Psychol Med* 42(4):843–853.
- Luo Y, Hawkley LC, Waite LJ, Cacioppo JT (2012) Loneliness, health, and mortality in old age: A national longitudinal study. Soc Sci Med 74(6):907–914.
- Cornwell EY, Waite LJ (2009) Social disconnectedness, perceived isolation, and health among older adults. J Health Soc Behav 50(1):31–48.
- Steptoe A, Breeze E, Banks J, Nazroo J (2012) Cohort Profile: The English Longitudinal Study of Ageing. Int J Epidemiol, 10.1093/ije/dys168.
- Hughes ME, Waite LJ, Hawkley LC, Cacioppo JT (2004) A short scale for measuring loneliness in large surveys: Results from two population-based studies. *Res Aging* 26(6):655–672.
- Pinquart M, Sorensen S (2001) Influences on Ioneliness in older adults: A meta-analysis. Basic Appl Soc Psych 23:245–266.

- Sugisawa H, Liang J, Liu X (1994) Social networks, social support, and mortality among older people in Japan. J Gerontol 49(1):S3–S13.
- US Census Bureau (2011) Current population survey, March and annual social and economic supplements, 2011. Available at www.census.gov/population/socdemo/ hh-fam/. Accessed June 25, 2012.
- McPherson M, Smith-Lovin L, Brashears ME (2006) Social isolation in America: Changes in core discussion networks over two decades. Am Sociol Rev 71:353–375.
- 34. European Social Survey (2010) Available at www.europeansocialsurvey.org/index. Accessed June 19, 2012.
- Office of National Statistics (2012) Families and Households, 2012. Available at www. ons.gov.uk/ons/dcp171778_284823.pdf. Accessed Jan. 22, 2013.
- Banks J, Karlsen S, Oldfield Z (2003) Socio-economic position. Health, Wealth and Lifestyles of the Older Population in England, eds Marmot M, Banks J, Blundell R, Lessof C, Nazroo J (Institute for Fiscal Studies, London), pp 71–125.
- Nicholson A, Kuper H, Hemingway H (2006) Depression as an aetiologic and prognostic factor in coronary heart disease: A meta-analysis of 6362 events among 146 538 participants in 54 observational studies. *Eur Heart J* 27(23):2763–2774.
- Pan A, Sun Q, Okereke OI, Rexrode KM, Hu FB (2011) Depression and risk of stroke morbidity and mortality: A meta-analysis and systematic review. JAMA 306(11): 1241–1249.
- Satin JR, Linden W, Phillips MJ (2009) Depression as a predictor of disease progression and mortality in cancer patients: A meta-analysis. Cancer 115(22):5349–5361.
- Steffick DE (2000) Documentation of Affective Functioning Measures in the Health and Retirement Study (Survey Research Center Univ of Michigan, Ann Arbor, MI).
- Cacioppo JT, Hawkley LC, Thisted RA (2010) Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychol Aging* 25(2):453–463.