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Association of cumulative loneliness with all-cause mortality among middle-aged and older adults in the United States, 1996 to 2019

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Loneliness is a growing public health concern worldwide. We characterized the association between cumulative loneliness and subsequent all-cause mortality, using data from 9,032 participants aged 50+ in the population-based US Health and Retirement Study (HRS) from 1996 to 2019. Loneliness status (yes; no) was measured biennially from 1996 to 2004, and we categorized the experience of cumulative loneliness over the 8-y period as never, one time point, two time points, and ≥three time points. A multivariable-adjusted age-stratified Cox proportional hazards regression model was fitted to examine the association between cumulative loneliness from 1996 to 2004 and all-cause mortality from 2004 to 2019. Excess deaths due to each category of cumulative loneliness were calculated. Compared to those who never reported loneliness from 1996 to 2004, participants experiencing loneliness at one time point, two time points, and ≥three time points respectively had 1.05 (95% CI: 0.96 to 1.15), 1.06 (95% CI: 0.95 to 1.19), and 1.16 (95% CI: 1.02 to 1.33) times higher hazards of mortality from 2004 to 2019 (*P* trend = 0.01). These results correspond to 106 (95% CI: 68 to 144), 202 (95% CI: 146 to 259), and 288 (95% CI: 233 to 343) excess deaths per 10,000 person-years, for those experiencing loneliness at each of one, two, or ≥three time points from 1996 to 2004. Cumulative loneliness in mid-to-later life may thus be a mortality risk factor with a notable impact on excess mortality. Loneliness may be an important target for interventions to improve life expectancy in the United States.

cumulative loneliness | mortality | excess death

Significance

Loneliness is a growing public health concern worldwide. In this population-based prospective cohort study, loneliness experienced over an 8-y period was associated with elevated mortality risk and excess deaths during the subsequent 15 y. Loneliness in mid-to-later life may be a potential intervention target to increase population life expectancy in the United States.

Loneliness is a growing public health concern worldwide. The US National Poll of Healthy Aging demonstrated that the prevalence of feeling isolated from others among adults aged 50 to 80 y doubled from 27% in 2018 to 56% in 2020 during the COVID-19 pandemic, and remained at 34% of older US adults in early 2023 (1). As the subjective experience of social isolation, loneliness is theorized as the discrepancy between desired social needs and actual social connection (2–5). Independently of the amount of objectively measured social isolation, loneliness has been associated with emotional stress (6, 7), unhealthy coping behaviors (5, 8), accelerated cognitive decline (9), and increased risk of cardiovascular disease and mortality among middle-aged and older adults (4, 10).

Although several studies have documented the association between loneliness and mortality, most have measured loneliness at a single point in time or over a short period of time (4, 11–17). The experience of loneliness may vary over time, as it may result from stressful life events that become more common in mid-to-later life, such as the loss of a spouse or occurrence of a serious health problem (3, 18, 19). Indeed, loneliness has been found to fluctuate over time among older adults (20–23), although few studies have considered its dynamic, time-varying nature over long periods of time during aging. This knowledge gap is significant and limits understanding of the true effect of loneliness on a range of health outcomes in later life. For example, short-term or intermittent loneliness could motivate positive coping strategies, such as reconnections with others, which may help to prevent against the adverse effect of loneliness, while prolonged loneliness may repeatedly trigger stress and vigilance responses, which could lead to a heightened cognitive and allostatic load, increased incidence of chronic health conditions, and premature mortality (24).

This study aimed to characterize the association between cumulative loneliness over an 8-y period from 1996 to 2004 and risk of all-cause mortality during the subsequent 15 y from 2004 to 2019 among adults aged 50+ in the United States. We hypothesized that greater cumulative loneliness would be associated with increased risk of subsequent all-cause mortality.

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The authors declare no competing interest.

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Results

This study included 9,032 participants, contributing 93,684 person-years of follow-up from 2004 to 2019 (Fig. 1). The median follow-up time was 10.37 y (interquartile range: 6.86 y). *SI Appendix*, Table S1 provides the full details of baseline characteristics according to cumulative loneliness. The mean age (SD) at baseline was 63.99 (8.62) years, and 62.51% (5,646) of the sample were women. Those who were younger, men, non-Hispanic White, married, working for pay, well educated, and wealthier were less likely to experience loneliness compared to their counterparts (all $P < 0.001$). A total of 5,514 (61.05%) participants never felt lonely, while 1,624 (17.98%), 825 (9.13%), and 1,069 (11.84%) experienced loneliness at one, two, and three or more time points during the 8-y exposure period from 1996 to 2004.

The Table 1 provides crude deaths per 10,000 person-years and the number of excess deaths from 2004 to 2019 according to the cumulative loneliness from 1996 to 2004. Experiencing loneliness at each of one, two, and three or more time points was respectively associated with 106 (95% CI: 68 to 144), 202 (95% CI: 146 to 259), and 288 (95% CI: 233 to 343) excess deaths per 10,000 person-years, compared to never feeling lonely.

The Table 1 presents multivariable-adjusted HRs and 95% CIs for the association between cumulative loneliness and subsequent all-cause mortality from the age-stratified Cox proportional hazards regression model. Compared to those who never reported loneliness, participants experiencing loneliness at one time point, two time points, and three or more time points respectively had 1.05 (95% CI: 0.96 to 1.15), 1.06 (95% CI: 0.95 to 1.19), and 1.16 (95% CI: 1.02 to 1.33) times higher hazards of mortality (P trend = 0.01; Fig. 2). However, the estimates for loneliness at one time point and two time points were imprecise with 95% CIs crossing the null. Estimates for all other covariates in the Cox proportional hazards regression model are shown in *SI Appendix*, Table S2.

Results from the sensitivity analyses supported our main findings. First, as we used a single item in the CES-D scale to measure loneliness, we restricted the analysis to individuals without depressive symptoms at baseline to ensure that our measure of loneliness did not simply reflect depressive symptoms. The restricted results were consistent with those from the main analysis, although the estimates were imprecise due to the smaller sample size (*SI Appendix*, Table S3). Second, to rule out potential reverse causation, we lagged the mortality outcomes to be from 2007 to 2019 and observed a somewhat stronger association between the loneliness experience and mortality (*SI Appendix*, Table S4). Third, because our use of self-reported loneliness status may lead to information bias due to loneliness underreporting, we used the 3-item UCLA Loneliness Scale in the Health and Retirement Study (HRS) 2006 as a gold standard to validate our measure of loneliness and performed a simple quantitative bias analysis to examine the robustness of our findings. *SI Appendix*, Table S5 shows the sensitivity and specificity values for our measure of loneliness against the gold standard. Simulation results from the quantitative bias analysis in *SI Appendix*, Table S6 indicate that we had over 85% probabilities of observing true HRs above the null for loneliness at each of one (86%), two (97%), and three time points or more (95%), suggesting that bias due to any potential underreporting of loneliness is unlikely to explain the observed results. We also repeated the model from the main analysis with bias-adjusted loneliness as a continuous variable (range 0 to 5), and results indicated that we had a 98% probability of observing a true HR above the null, providing strong evidence for the trend of the association between cumulative loneliness and mortality risk (*SI Appendix*, Table S6). Finally, results were consistent when we restricted the modeling analysis to individuals with inverse probability of treatment weights less than 5.0 (*SI Appendix*, Table S7).

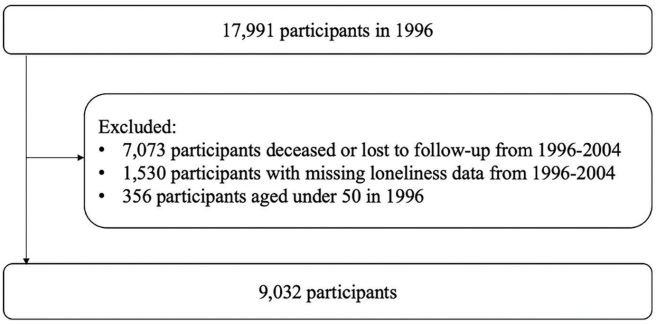

Fig. 1. Study flow diagram, the US Health and Retirement Study, 1996 to 2019.

Discussion

In this population-based prospective cohort study, loneliness experienced over an 8-y period was associated with higher mortality and excess deaths during the subsequent 15 y among middle-aged and older adults in the United States. These findings indicate that public health initiatives and policies to reduce the experience of loneliness among aging adults may hold promise for increasing population life expectancy.

Comparison with Existing Studies. Consistent with existing studies (11–17), we found that the experience of loneliness was associated with higher risk of all-cause mortality and a greater number of excess deaths. Our findings add to the existing literature by demonstrating that the cumulative experience of loneliness over time could be an important risk factor for mortality. Biological plausibility for the association between loneliness and mortality is supported by emerging evidence. Loneliness may induce dysregulation of systemic inflammation (25), elevated blood pressure (26), accelerated memory aging (9), and worse cardiovascular health (27), leading to premature mortality. Loneliness has been associated with poor health outcomes and increased health care utilization, such as hospitalization and emergency visits, among individuals with heart failure (28). Recent research has also shown that the experience of loneliness was associated with higher odds of death at 30 d among individuals undergoing nonelective surgery (29). These findings indicate the importance of loneliness in both health care and community settings. Potential interventions, such as those through supportive social networks, physical activity, and animal therapy, hold promise to ameliorate loneliness, while further investigation is warranted given the inconsistent findings in the current literature, the challenge of intervention design, and the complexity of loneliness (30, 31).

This study contributes to the existing literature by indicating that the experience of loneliness is not consistent over time and that its association with mortality varies by its frequency. Hence, our findings may help to explain the inconsistent results from the current literature, whereby a number of previous studies that measured loneliness cross-sectionally or over short periods of time observed small and nonstatistically significant effects of loneliness on mortality (4, 15, 32). The measurement of loneliness at a single point in time or over short periods of time may not accurately reflect the time-varying nature of this exposure, and previous results on this topic may thus be subject to bias due to inadequate measurement.

Limitations and Strengths. This study has limitations. First, although the HRS has tried to increase the accuracy of mortality

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Table 1. Excess deaths from 2004 to 2019 and multivariable-adjusted HRs (hazard ratios) according to the experience of cumulative loneliness from 1996 to 2004 in the US Health and Retirement Study, 1996 to 2019, (N = 9,032)

	Cumulative loneliness			
	Never	One time point	Two time points	≥Three time points
No. of deaths	2,386	834	472	667
No. of participants	5,514	1,624	825	1,069
Person-years (PYs)	59,660	16,488	7,839	9,696
Deaths per 10,000 PYs	400	506	602	688
Excess deaths per 10,000 PYs (95% CI)*	Ref.	106 (68 to 144)	202 (146 to 259)	288 (233 to 343)
Adjusted HR (95% CI)†	Ref.	1.05 (0.96 to1.15)	1.06 (0.95 to 1.19)	1.16 (1.02 to 1.33)
P trend‡				0.01

*Excess deaths represent differences in the number of deaths per 10,000 person-years between each of the loneliness experience group and the reference group.
†The age-stratified Cox proportional hazards model was fitted to estimate the association between cumulative loneliness and all-cause mortality, adjusted for gender, race/ethnicity, marital status, education, employment status, household wealth, objective social isolation index, obesity, CES-D (Center for Epidemiologic Studies Depression) scores, ADL (activities of daily living) scores, self-rated health, and the number of comorbid diseases. Age (in categories of 50 to 54; 55 to 59; 60 to 64; 64 to 69;70 to 74; 75 to 79; 80+) was stratified to meet the proportionality assumption. Inverse probability of treatment weighting (IPTW) was incorporated to account for time-varying confounders from 1996 to 2004.
‡*P* trend was derived from the age-stratified Cox proportional hazards model with the cumulative loneliness as a continuous variable (range 0 to 5).

data as best as possible, the death data were not directly from the National Death Index and our results could be subject to nondifferential misclassification bias of the mortality outcome, which may bias our results toward the null (33, 34). Second, we did not measure within-person trajectories of the loneliness experience as it is beyond the scope of this study. Rather, we captured loneliness as the number of HRS waves over an 8-y period in which each respondent reported loneliness. While this count measure largely reflects the degree to which loneliness is cumulative over time, it may not capture a heterogeneous range of loneliness experiences in terms of their timing, duration, and intensity over time. Further research is warranted to investigate these more nuanced aspects of the loneliness experience during aging and its association with mortality outcomes among older adults. Finally, participants were required to be retained in the study from 1996 to 2004 to have complete loneliness data. Hence, our findings may be subject to selection bias if individuals experiencing greater loneliness and elevated mortality were more likely to drop out from the study during this period, a scenario which would lead to an underestimation of the effect of the loneliness experience on mortality.

This study has several strengths. It is one of the few that has measured the long-term experience of loneliness and its association with subsequent all-cause mortality over a 15-y follow-up in a population-based sample. Although self-reported loneliness may involve measurement error, we assessed loneliness status at five time points to classify its long-term experience and reduce within-person variance. Our quantitative bias analysis using a simulation model to correct our measure of loneliness according to its sensitivity and specificity value when using the 3-item UCLA Loneliness Scale as a gold standard supported the conclusion that potential underreporting of loneliness does not meaningfully impact our results. Finally, we observed a dose–response relationship between a greater number of time points with loneliness and subsequent mortality, which supports biological plausibility and indicates that this association requires further confirmation in other populations and settings.

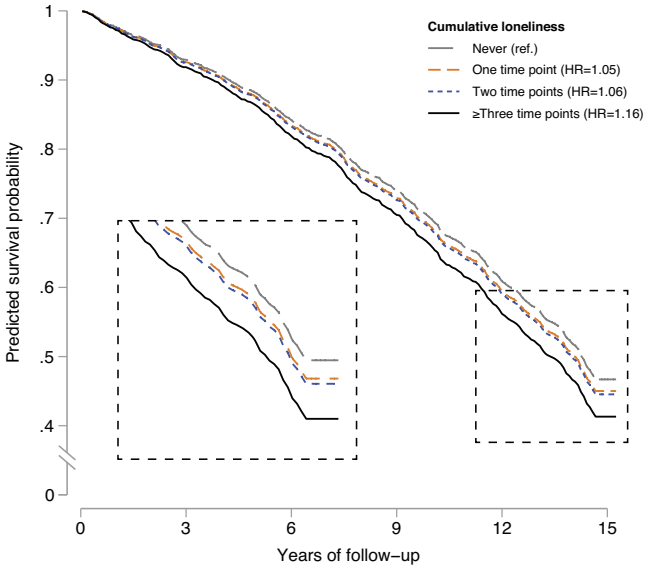

Fig. 2. Kaplan–Meier survival curves by cumulative loneliness from 1996 to 2004 among individuals aged 60 to 64 at baseline, the US Health and Retirement Study, 1996 to 2019, N = 9,032. Note: The predicted survival probabilities were estimated based on the adjusted HRs from the age-stratified Cox proportional hazards model in Table 1. Covariates are held at their mean values or at their reference categories. Age group is held at 60 to 64 y. The survival curves for loneliness at one time point and two time points overlap due to similar HRs. Kaplan–Meier survival curves for the other age groups (50 to 54; 55 to 59; 65 to 69; 70 to 74; 75 to 79; 80+) are provided in *SI Appendix*, Figs. S1–S6.

Material & Methods

Data Source, Study Design, and Study Sample. Data were from the US HRS from 1996 to 2019. The HRS is a population-based longitudinal cohort study of over 20,000 adults aged 50 and over in the United States since 1992. It has been approved by the University of Michigan Institutional Review Board in the United States (IRB number: HUM0061128) (35). Multistage probability sampling strategy was used to select eligible participants across the United States with face-to-face and telephone-based interviews conducted biennially. Written informed consent was obtained from all study participants. Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

The present prospective cohort study used data from the HRS to measure the loneliness experience from 1996 to 2004 and mortality during the subsequent 15 y from 2004 to 2019. Participants who 1) were aged 50 and over in 1996, 2) remained alive in the study in 2004, and 3) had complete data on loneliness from 1996 to 2004 were eligible for inclusion (N = 9,032, see Fig. 1 for the study flow diagram).

Measures.

Exposure: Cumulative loneliness from 1996 to 2004. At each biennial interview wave, individuals were asked to answer the question "do you feel lonely?" (yes vs. no), which is an item from the 8-item CES-D Scale (36, 37). We defined cumulative loneliness according to the experience of loneliness over five HRS waves from 1996 to 2004: never, one time point, two time points, and three or more time points (9). We combined individuals with the experience of loneliness at three (n = 525), four (n = 213), and five time points (n = 135) to maintain adequate sample size.

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Outcome: All-cause mortality from 2004 to 2019. All-cause mortality was measured from 2004 to 2019. The HRS identifies death cases from a next-of-kin in the HRS exit interviews or from other sources (e.g., spouse's core interview) (38). The mortality data in HRS have been validated using the National Death Index (accuracy >95%) (38). As not all HRS interviews are finished in the same calendar year (e.g., 2004 and 2005 for the 2004 survey), the beginning of the follow-up for each person was defined as their interview month of the 2004 data collection wave in the year of 2004 or 2005 (39). For those who died, person-years of follow-up were calculated as the interval between the 2004 study interview month and the month of the year when the death event was recorded (n = 4,359). Individuals lost to follow-up without a death record were censored in the most recent available month of the year that the HRS was able to confirm their alive status, e.g., from spouse interviews (n = 1,226). Participants who were followed up until the 2018 data collection wave (n = 3,447) were censored in the month of their 2018 interview (in the year 2018 or 2019).

Covariates in 1996. We included the following covariates, measured at baseline in 1996, as potential confounders (4, 15–17, 20). Sociodemographic characteristics included age (in categories of 50 to 54; 55 to 59; 60 to 64; 65 to 69; 70 to 74; 75 to 79; 80+), gender (woman vs. man), race/ethnicity (Non-Hispanic White; Non-Hispanic Black; other/unknown), marital status (married/partnered; separated/divorced; widowed; never married), education (less than high school; general education diploma; high school; some college; college and above), employment status (working for pay; not working for pay), and household wealth (in quintiles). Consistent with a prior study (9), we controlled for an objective social isolation index (range: 0 to 5) with higher scores indicting higher social isolation (4, 15–17, 20). This objective social isolation index incorporated the number of persons in the same household, the number of good friends in the neighborhood, the number of relatives in the neighborhood, the frequency of volunteer work for religious or other charitable organizations, and the frequency of getting together with any of participants' neighbors. Obesity (yes; no) was defined as values of body mass index higher than 30 kg/m^2 (40). Baseline health conditions were measured as the number of comorbid diseases including self-reported hypertension, diabetes, cardiovascular disease, stroke, and cancer (range: 0 to 5). Self-rated health was categorized as excellent, very good, good, fair, or poor. Finally, we assessed depressive symptoms using CES-D scores (range: 0 to 7, excluding the loneliness item score) and number of limitations to ADLs (range: 0 to 5).

Statistical Analysis. We performed descriptive analyses including ANOVA, Pearson chi-square test, and Kruskal–Wallis rank sum tests to examine baseline characteristics by cumulative loneliness. We calculated excess mortality according to cumulative loneliness. To estimate the multivariable-adjusted association between cumulative loneliness and mortality, we calculated HRs, i.e., the ratio of instantaneous hazard rates of death between two groups, from a Cox proportional hazards regression model (41). We fitted an age-stratified Cox proportional hazards regression model, as age did not meet the proportionality assumption. IPTW was incorporated in modeling to account for time-varying confounders from 1996 to 2004 that could also be mediators on the pathway between loneliness and mortality, such as marital status, depressive symptoms, objective social isolation index, and the number of comorbid diseases. Details are provided in *SI Appendix, Method* and Table S8.

As women could be more likely than men to experience loneliness (4), we tested gender differences in the association under study by including a statistical interaction term between cumulative loneliness and gender. Because older adults may have limited material or emotional resources than younger adults with which to prevent against the adverse effects of loneliness (9, 14, 42), we also tested for effect modification by age using statistical interaction terms between cumulative loneliness and age groups. These interaction terms were not statistically significant ($P > 0.05$) and therefore not retained in the analyses (see *SI Appendix*, Table S9 for results of the interaction analyses). All analyses were performed with Stata/SE 18.0.

Sensitivity Analysis. We performed four sensitivity analyses to examine the robustness of our findings. First, we restricted the analyses to individuals without depressive symptoms at baseline (CES-D scores lower than three) to rule out the possibility that loneliness simply reflected depressive symptoms. Second, we restricted the follow-up period from 2004 to 2019 to 2007 to 2019 to allow for a longer latency period, as loneliness may not have an acute impact on individuals' mortality outcomes. Third, we performed a quantitative bias analysis to evaluate whether any potential differential underreporting of loneliness according to mortality status could bias the results (43), as the single item of loneliness from the CES-D Scale may be subject to stigma-related underreporting during the study interviews (44). We used the 3-item UCLA Loneliness Scale from the HRS 2006 Leave Behind Questionnaire as the gold standard for assessing loneliness, due to its greater number of items with no questions mentioning "loneliness" and its private pen-and-paper mode of data collection (44, 45). We used the 3-item UCLA Loneliness Scale to calculate sensitivity and specificity values of our loneliness measure, according to mortality. We corrected cumulative loneliness status at the record level according to these sensitivity and specificity values and re-ran our analysis 100 times to evaluate whether any potential misclassification of the cumulative loneliness experience could influence our results (details are provided in *SI Appendix*, Tables S5 and S6). Finally, we restricted the analyses to individuals with IPTW <5.0 to rule out any impacts of large values of IPTW.

Conclusion

This population-based longitudinal study of aging US adults found that cumulative loneliness may be a meaningful risk factor for mortality in mid-to-later life. Ameliorating the loneliness experience in mid-to-late life could be a potential intervention target to reduce excess deaths and increase life expectancy in the United States.

Data, Materials, and Software Availability. The HRS data are publicly available at https://hrs.isr.umich.edu/about (35). X.Y. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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