**Social Isolation and Mortality among Married Couples and by Spousal Dyad Characteristics**

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AUTHORS: Please add/edit your name, highest degree, institutional information, COI statement, and financial disclosure below

author order is tentative

Kassandra I. Alcaraz, PhD

Department, Institution, City, State

COI Statement

Financial Disclosure

Matthew Masters, MPH

Population Science, American Cancer Society, Atlanta, GA

COI Statement

Financial Disclosure

Monica L. Baskin, PhD

Department, Institution, City, State

COI Statement

Financial Disclosure

Regine Haardörfer, PhD

Behavioral, Social, and Health Education Sciences, Emory University, Atlanta, GA

Regine Haardörfer declares no Conflict of Interest

Regine Haardörfer has no Financial Disclosures

Tiffany L. Carson, PhD

Department, Institution, City, State

COI Statement

Financial Disclosure

W. Dana Flanders, MD, DSc

Department of Epidemiology, Emory University, Atlanta, GA 30322

COI Statement: Dr. Flanders declares no conflicts

Financial Disclosure: Dr. Flanders owns Epidemiologic Research & Methods, which provides consulting services for various corporate clients. None of the consulting work is related to this paper.

J. Lee Westmaas, PhD

Population Science, American Cancer Society, Atlanta, GA

J. Lee Westmaas declares no Conflicts of Interest

J. Lee Westmaas has no Financial Disclosures

Robert Stephens, PhD

Department, Institution, City, State

COI Statement

Financial Disclosure

Sicha Chantaprasopsuk, MPH

Department, Institution, City, State

COI Statement

Financial Disclosure

Susan M. Gapstur, PhD

Consultant, Tiffin, IA

Susan M. Gapstur declares no Conflicts of Interest

Susan M. Gapstur had no Financial Disclosure

Corresponding Author: KA Name, Physical Address, Phone, Fax, Email

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**ABSTRACT** max. 250 words.; currently 249; must include years of data and years of analysis

**Introduction:** Social isolation is associated with greater mortality, and marriage is associated with reduced risk, although sex differences are documented. The social isolation-mortality association within marriage is understudied. This study investigated associations of married person’s social isolation with his/her mortality risk and his/her spouse’s mortality risk, and whether associations vary by spousal isolation concordance.

**Methods:** The study used longitudinal data from a cohort of U.S. adults containing 143,663 opposite-sex spousal dyads (287,326 individuals). A modified Social Network Index was used to assess social isolation. In 2020, multivariable Cox proportional hazard regression examined associations of social isolation with all-cause, cancer, and cardiovascular disease (CVD) mortality over 34 years of follow up (1982-2016).

**Results:** Men were more socially isolated than women. Associations of social isolation and mortality were observed (HRs=1.04 to 1.23) and generally attenuated with time. Having a socially isolated spouse was associated with all-cause mortality (HR=1.05) and cancer mortality (HR=1.06). Compared to being in a dyad in which neither spouse was socially isolated, being in a dyad in which only the husband was isolated resulted in higher all-cause mortality for men (HR=1.15) but not women. Being in a dyad in which only the wife was isolated, or in which both spouses were isolated, resulted in higher all-cause mortality for both spouses (HRs=1.11 to 1.19). Findings for cancer mortality and CVD mortality were more nuanced.

**Conclusions:** Social isolation influences mortality within marriage, especially affecting men. A holistic approach to understanding social isolation, such as couple-based assessment or intervention, may reduce mortality risk.

**INTRODUCTION**

Social isolation, indicated by limited human connections and interactions (House 1988) is a strong and independent risk factor for death (Alcaraz),), increasing mortality risk as much as or more than clinical risk factors such as obesity (Pantell 2013; Holt-Lunstad 2015). Conversely, marriage—reflecting one type of social connection—is associated with better health and lower mortality (Rendall 2011; Robards 2012). However, the extent to which social isolation influences health outcomes *within* marriage is less clear. Elucidating the social isolation-mortality association can provide guidance for addressing social influences on health, a critical need given the growing demand to increasingly consider social risks in clinical care (Fitchenberg 2019; Alcaraz 2020; NASEM 2019; Lunstad 2020; CMS).

The U.S. national prevalence of social isolation is not well documented (due to lack of systematic measurement in U.S. health surveys), but recent studies estimate one-fourth to one-half of adults ages 60 years or older are socially isolated (Cudjoe 2018; Fakoya 2020; NASEM 2020). It is likely that the U.S. prevalence of social isolation is considerably higher (Holt-Lunstad 2017) because these estimates do not include younger adults and stigma associated with social isolation results in underreporting (CITE). In addition, social isolation is disproportionately higher in socioeconomically disadvantaged populations, the chronically ill, and racial/ethnic minority groups (Alcaraz 2019; KFF 2018). Therefore, identifying strategies to address social isolation can enhance public health and foster health equity.

Social isolation is hypothesized to influence mortality through multiple pathways, including by impacting mental and emotional health, health behavior, social support, healthcare utilization and treatment adherence, and inducing physiological or epigenetic changes (Yang 2016; Holt-Lunstad 2015; House 2001). Similar mechanisms likely contribute to the protective effect of marriage on health (CITE). In fact, marital status is a typical component of social isolation measurement. Evidence suggests much of the influence of social isolation on mortality is attributable to being unmarried (Berkman 1979; Berkman 2004), although composite social isolation measures are better predictors of mortality than marital status alone. Questions remain regarding the influence of social isolation on mortality among married individuals and whether social isolation influences mortality similarly for women and men.

The overall association of social isolation with mortality is well established, yet sex differences in the social isolation-mortality association are less clear. Several studies report similar associations of social isolation and all-cause mortality for women and men (Barger 2013; Steptoe 2013; Laugeusen 2018). However, other studies report stronger associations among men compared to women (House 1988; Kaplan 1988; Yang 2013). One possible driver of this sex difference is that the health and mortality benefits of marriage are stronger for men than women (Kiecolt-Glaser 2001; Wanic 2011; Robards 2012). A recent analysis of National Center for Health Statistics data on adults ages 25 years or older reports that, among women and men of all marital status groups, age-adjusted death rates are lowest for married men and highest for widowed men (Curtin 2019). Unfortunately, many studies investigating the social isolation-mortality association lack sufficient statistical power for subgroup analyses (Berkman 2004; Schoenbach 1986; Reynolds 1990), underscoring the need for additional research in this area.

Examining social isolation among married couples presents a unique opportunity to fill existing knowledge gaps. Research with spouses can provide insight into the disadvantage of being socially isolated versus the advantage of being married as well as possible differences by sex. Additionally, unlike merely examining marital status, examining spousal characteristics (many of which are modifiable) can inform targeted intervention development. Prior research found, for example, that characteristics of an individual can influence his/her spouse’s longevity (Stavrova 2019), cardiovascular disease risk (Quintana 2015), and health-related quality of life (among couples with cancer) (Litzelman 2016). Accordingly, an individual’s socially isolation status may influence his/her spouse’s mortality risk.

**Study aims**

This study investigated (1) associations of a married person’s social isolation with his/her mortality risk and his/her spouse’s mortality risk and (2) whether associations vary by spousal isolation concordance. The use of data from a large U.S.-based cohort containing a large number of spousal dyads allows for the examination of sex differences and multiple mortality outcomes.

**METHOD**

The study used data from the American Cancer Society’s Cancer Prevention Study II (CPS-II), a longitudinal cohort study of adults in the United States. In 1982 and 1983, 1,184,284 adults aged 30 years or older were enrolled into CPS-II in all 50 U.S. states, the District of Columbia, and Puerto Rico. Participants completed and returned via mail a self-administered questionnaire (Calle EE 2002). The CPS-II protocol was approved by the Institutional Review Board of Emory University.

**Study sample**

Participants who, at the time of enrollment, reported a personal history of heart disease, cancer, stroke, or chronic obstructive pulmonary disease (n = 233,708) were excluded from analysis to eliminate possible bias due to reverse causality. Participants with missing or non-numeric social isolation data also were excluded (n = 327,033), as were participants with incomplete smoking data (n = 31,150). Men over age 90 and women over age 95 at baseline (n = 201) were excluded as well because some deaths are missed by National Death Index linkage, which may result in significant misclassification of vital status (Calle 1993, Jacobs 2018). Lastly, participants who were unmarried at baseline (n = 124,608) or had their spouse excluded due to the above criteria (n = 180,258) were excluded. These exclusions resulted in an analytic sample of 287,326 married individuals, or 143,663 opposite-sex spousal dyads.

**Measures**

Social isolation.Social isolation was assessed using Social Network Index (Berkman 1979) items on frequency of church/temple attendance, frequency attending club meetings or group activities, and number of friends or relatives the respondent feels close to. Marital status is a typical Social Network Index item, but as all participants in this study were married at baseline, this item was excluded. As in prior studies, we scored each item 0 (not isolated) or 1 (isolated), basing the score for the close friend item on the frequency distribution of responses (Liu, 2011; Reynolds, 1990; Alcaraz 2019). Participants reporting attending church/temple (hereafter described as “religious services”) at least once per month were assigned a score of 0; others were assigned a score of 1. Participants reporting attending club meetings or group activities at least once per month were assigned a score of 0; others were assigned a score of 1. Participants reporting having 7 or more close friends or relatives were assigned a score of 0; others were assigned a score of 1.

Scores for the three items were used to compute a social isolation score. Consistent with other Social Network Index studies (e.g., Kaplan 1988; Reynolds 1990), we weighted each item equally. Social isolation scores ranged from 0 (least isolated) to 3 (most isolated). To facilitate planned analyses, a dichotomous isolation variable was created by coding participants with social isolation scores of 0 or 1 as not isolated (0) and participants with scores of 2 or 3 as isolated (1).

Spousal isolation concordance.Spousal isolation concordance was based on dichotomized social isolation status (isolated/not isolated). Four categories were coded based on whether neither spouse was isolated, only the husband was isolated, only the wife was isolated, or both spouses were isolated.

Mortality.Cause of death has been for more than 99% of all deaths. From 1982 through 1988, personal inquiries were made to determine participants’ vital status and place/date of deaths, if applicable, and death certificates subsequently were obtained for verification. After 1988, information from the National Death Index was used to identify deaths through December 2016, as well as deaths among the 21,704 participants lacking follow up between 1982 and 1988. Follow-up time was the period of time from completion of the baseline questionnaire to the date of death, age 90 years for men or 95 years for women, or December 31, 2016 (whichever came first).

Individual characteristics. Individual characteristics were sex, age, race/ethnicity, education level, baseline smoking status (never smoker, current smoker, former smoker, ever pipe/cigar smoker), history of diabetes mellitus (yes/no), and baseline body mass index (BMI). BMI was calculated from self-reported height and weight (weight (kg) divided by squared height (m2), and categorized according to standard BMI categories (CITE) (normal/healthy weight, underweight, overweight, obese, missing).

Dyad characteristics.Dyad characteristics were interracial marriage status and residency type. Dyads in which spouses were of the same race/ethnicity were coded as in an interracial marriage; other dyads were coded as not in an interracial marriage. Residency type was based on each spouse’s address as provided in the baseline survey in 1982/1983. Using 1983 Rural-Urban Continuum Codes (RUCC) (CITE), dyads were coded as rural (RUCC of 4 through 9), urban (RUCC of 0 through 3), mismatched (one urban-dwelling spouse, one rural-dwelling spouse), or missing (geolocation algorithm unable to identify address with sufficient accuracy).

**Statistical Analyses**

Hereafter, actor-partner terminology (CITE) is used to differentiate between an individual (actor) and his/her spouse (partner).

Bivariate and preliminary analyses.Bivariate analyses compared sample characteristics by social isolation status using the dichotomized isolation variable. Preliminary analyses informed the final model-building approach. First, given that individuals are clustered within dyads, we hypothesized that social isolation scores would be correlated within dyads. This hypothesis was supported by high ICCs [Matt: please add a brief ICC summary here (MM: see comment)] for the four-point social isolation score and Pearson’s correlation and Cohen’s Kappa tests using the dichotomous isolation variable [Matt: please briefly summarize correlations here (MM: see comment)]. These findings supported a multilevel modeling approach, consistent with previous longitudinal research using spousal dyads (Stavrova 2019).

Second, we observed a violation of the proportional hazards assumption, which was expected given that social isolation was assessed at baseline and analyses predicted mortality over a 34-year follow-up period. Therefore, similar to a previous CPS-II social-isolation-mortality study (Alcaraz),), we examined associations of social isolation and mortality outcomes (all-cause, cancer, and CVD) in two follow-up periods: 1982-1999 and 2000-2016. To confirm proportional hazards in these follow-up periods, we computed *P-values* for multiplicative interactions with time for isolation scores and assessed log(-log(Survival)) curves for parallelism. After splitting follow-up time, all *P-values* for time and isolation interactions were non-significant (at p<0.05) and log(-log(Survival) plots showed sufficient parallelism.

Aim 1 analyses.First, associations of actor social isolation and partner social isolation, separately, with risk of actor mortality were examined. Multilevel Cox proportional hazards regression models were constructed for the three mortality outcomes (all-cause, cancer, CVD) and both follow-up periods (1982-1999, 2000-2016). Models controlled for age, race/ethnicity, education level, smoking status, history of diabetes, and BMI. To account for dyadic correlations in outcomes, we used the robust sandwich variance estimation method and shared frailty method using a log-normal distribution (Therneau, 2020). Both actor isolation and actor sex were strong confounders of partner isolation on mortality; therefore, both were included in subsequent models. Exploratory models investigated two dyad characteristics—interracial marriage status and residency type—as predictors of actor social isolation.

Aim 2 analyses.Second, given sex differences in both the adverse effect of social isolation and the salubrious effect of marriage, associations of isolation with mortality risk for male and female actors by spousal isolation concordance was examined. Notably we wanted to distinguish whether the isolated spouse was the husband or the wife. While robust sandwich estimation and frailty models allow examination of dyadic variables, their usage in dyadic models with distinguishable members (e.g., husbands versus wives) is questioned (Kenny, 2007). Stratified models maintain independence of observations and allow for differing variances between the distinguishing characteristic (in this study, actor sex). To this end, sex-stratified Cox proportional hazards models were employed for Aim 2. Models controlled for age, race/ethnicity [Matt: true? see Table 4], education level, smoking status, history of diabetes, and BMI.

Multivariable hazard ratios and 95% confidence intervals are reported for all models. Analyses were conducted in 2020 using R version 4.0.2 using the *survival* package for survival models, and the *lme4* and *psych* packages for ICC and Cohen’s Kappa calculation.

**RESULTS**

**Sample characteristics**

The sample was predominantly non-Hispanic white, most participants had at least a high school education, and lived in urban settings (Table 1). Social isolation was associated with all individual demographic and health characteristics assessed (Table 1). Males were more socially isolated than females (Table 2).

**Social isolation and mortality**

Table 3 presents associations of actor social isolation and partner social isolation with actor mortality.

Actor isolation and actor mortality. In the first follow-up period, actor isolation was associated with each mortality outcome (all-cause: HR=1.15; 95% CI=1.12, 1.18; cancer: HR=1.10; 95% CI=1.05-1.15; CVD: HR=1.13; 95% CI=1.08, 1.18). These associations were slightly attenuated in the second follow-up period but remained statistically significant.

Partner isolation and actor mortality.In the first follow-up period, individuals with an isolated spouse had 5% higher all-cause mortality (HR=1.05; 95% CI=1.02, 1.08) compared to those with a non-isolated spouse. However, this association was attenuated and nonsignificant in the second follow-up period. Similarly, individuals with a socially isolated spouse had 6% higher cancer mortality (HR=1.06; 95% CI=1.01, 1.11) compared to those with a non-isolated spouse. This association was attenuated in the second follow-up period but remained statistically significant. No associations of partner social isolation and actor mortality were observed for CVD mortality in either follow-up period.

Dyad characteristics.Interracial marriage status was not associated with any actor mortality outcome for either follow-up period. However, analyses identified several associations of residency type with mortality outcomes. In the second follow-up period, rural-dwelling spouses had higher all-cause mortality (HR=1.04; 95% CI=1.02, 1.07) and CVD mortality (HR=1.07; 95% CI=1.03, 1.10) than urban-dwelling spouses. Additionally, in the first follow-up period, spouses with a mismatched residency type (i.e., one urban-dwelling, one rural-dwelling) had higher all-cause mortality (HR=2.91; 95% CI=2.04, 4.14), cancer mortality (HR=2.88; 95% CI=1.74, 4.79), and CVD mortality (HR=2.70; 95% CI=1.53, 4.76) than urban-dwelling couples. [Authors: I’m considering cutting part or all of this section. Not sure it adds much except possibly informing future work. Also the Ns for residency type mismatches are tiny (see Table 1). Thoughts?]

**Spousal isolation concordance and mortality**

Table 4 presents multivariable, sex-stratified models of social isolation and mortality based on categories of spousal isolation concordance.

All-cause mortality.In the first follow-up period, compared to men in dyads in which neither spouse was isolated, men in dyads with at least one isolated spouse had higher all-cause mortality. Specifically, men in husband-isolated dyads had 15% higher all-cause mortality (HR=1.1500; 95% CI=1.1123, 1.890), men in wife-isolated dyads had 12% higher all-cause mortality (HR=1.1157; 95% CI=1.0535, 1.1816), and men in both-isolated dyads had 20% higher all-cause mortality (HR=1.1999; 95% CI=1.1486-1.2536). In the second follow-up period, these associations were attenuated but remained statistically significant in husband-isolated and both-isolated dyads.

In the first follow-up period, compared to women in dyads in which neither spouse was isolated, women in dyads in which only the wife was isolated or in which both spouses were isolated had higher all-cause mortality. Specifically, women in wife-isolated dyads had 18% higher all-cause mortality (HR=1.1776; 95% CI=1.0880-1.2745) and women in both-isolated dyads had 17% higher all-cause mortality (HR=1.1748; 95% CI=1.1033-1.2509). In the second follow-up period, these associations were attenuated but remained significant in both-isolated dyads. Women in dyads in which only the husband was isolated did not have higher all-cause mortality than women in dyads in which neither spouse was isolated in either follow-up period.

Cancer mortality.In the first follow-up period, compared to men in dyads in which neither spouse was isolated, men in dyads with at least one isolated spouse had higher cancer mortality. Specifically, men in husband-isolated dyads had 13% higher cancer mortality (HR=1.1285; 95% CI=1.0674-1.1932), men in wife-isolated dyads had 11% higher cancer mortality (HR=1.1053; 95% CI=1.0054-1.2152), and men in both-isolated dyads had 16% higher cancer mortality (HR=1.1615; 95% CI=1.0797-1.2495). In the second follow-up period, these associations were attenuated but remained statistically significant in husband-isolated dyads.

In the first follow-up period, compared to women in dyads in which neither spouse was isolated, women in dyads in which both spouses were isolated had higher cancer mortality. Specifically, women in both-isolated dyads had 12% higher cancer mortality (HR=1.1247; 95% CI=1.0204-1.2400). This association was similar in the second follow-up period (HR=1.1326; 95% CI=1.0509-1.2206). Women in dyads with only one isolated spouse did not have higher cancer mortality than women in dyads in which neither spouse was isolated in either follow-up period.

CVD mortality. In the first follow-up period, compared to men in dyads in which neither spouse was isolated, men in dyads in which only the husband was isolated or in which both spouses were isolated had higher CVD mortality. Specifically, men in husband-isolated dyads had 11% higher CVD mortality (HR=1.1078; 95% CI=1.0500-1.1689) and men in both-isolated dyads had 13% higher CVD mortality (HR=1.1300; 95% CI=1.0521-1.2137). In the second follow-up period, the association in husband-isolated dyads was attenuated yet remained statistically significant, and the association in both-isolated dyads was similar to the association observed in the first-follow-up period (HR=1.1203; 95% CI=1.0525-1.1925).

In the first follow-up period, compared to women in dyads in which neither spouse was isolated, women in dyads in which only the wife was isolated or in which both spouses were isolated had higher CVD mortality. Specifically, women in wife-isolated dyads had 22% higher CVD mortality (HR=1.2196; 95% CI=1.0583-1.4056) and women in both-isolated dyads had 17% higher CVD mortality (HR=1.1732; 95% CI=1.0481-1.3132). In the second follow-up period, these associations were attenuated but remained statistically significant in both-isolated dyads. Women in dyads in which only the husband was isolated did not have higher CVD mortality than women in dyads in which neither spouse was isolated in either follow-up period.

**DISCUSSION**

Using longitudinal data from a large cohort of U.S. adults, social isolation was associated with greater mortality among married individuals. Additionally, having a socially isolated spouse was associated with higher risk of death after accounting for other risk factors. To our knowledge, this is the first study examining the influence of social isolation on a spouse’s mortality risk and investigating the contextual nature of this association within marriage.

Among married individuals, the overall increased mortality risk of having a socially isolated spouse was relatively small: 5% for all-cause mortality and 6% for cancer mortality. Additionally, overall each mortality outcome was more strongly associated with an individual’s own social isolation (HRs 1.10-1.15 in the first follow-up period) than his/her spouse’s isolation. However, as cancer and cardiovascular disease are the leading causes of death in the U.S. (NCHS 2020), excess mortality—regardless of size or source—can have significant impact at the population level, especially given that a significant proportion of the U.S. population may be socially isolated (Holt-Lunstad 2017).

Findings on sex differences can inform intervention strategies with the socially isolated. In most models, both spouses being isolated was associated with the highest risk of mortality compared to other categories of spousal isolation concordance. This pattern is consistent with prior studies documenting a dose-response relationship of social isolation with mortality, with more isolation associated with greater mortality risk (CITE incl. Alcaraz 2019). Therefore, married individuals in dyads in which both spouses are socially isolated may derive the most benefit from social isolation intervention.

Men appear to be another vulnerable group. Mortality risk for married men was influenced not only by their own social isolation but also by their wives’ isolation, in many cases even after more than three decades of follow up. In addition, the effect on husbands’ mortality was similar regardless of which spouse was isolated, whereas wives’ mortality was influenced less by husbands’ mortality. Only when wives themselves were isolated did wives’ mortality risk increase. Scant research has examined an individual’s characteristics as predictors of spousal mortality. Some findings from the current study are consistent with a small body of research on associations between an individual’s characteristics and his/her spouse’s mortality. Studies that predict mortality based on one’s spouse’s socioeconomic characteristics consistently report overall associations, yet findings on sex differences are mixed (Yang 2011; Skalicka 2008; CITE). A dyadic study of 4374 elderly spouses found an individual’s life satisfaction to be inversely associated with his/her spouse’s mortality (Stavrova 2019), although no sex differences were observed.

The study’s identification of an interpersonal effect of social isolation and mortality among spouses is novel, although spousal influences have been observed in other studies. Research has found that spouses influence each other’s health behaviors (Falba 2008; Homish 2008; Jackson 2015; CITE), mental well-being (CITE), and self-rated health (Brown 2013; CITE). Prior research also has reported sex differences in the influence of social networks. A study of smokers found that social network influences positively affected men’s quitting behavior more than women’s (Westmaas 2002). [ADD ANOTHER] Additional research is needed to identify mechanisms driving spousal and social network influences among socially isolated individuals. For example, factors such as marital satisfaction may moderate spousal influence (CITE), and the protective effect of marriage is reduced as individual health worsens (CITE).

The evolving healthcare landscape reflects an increasing recognition of social determinants of health (CITE) and growing integration of social care and health care (NASEM 2019). However, patients’ social history often remains neglected in the clinical encounter (CITE). These trends necessitate research to identify social risk-focused interventions that can be adopted in clinical settings (Fitchenberg 2019). Recommended strategies to understand and address social isolation predominantly focus on an individual’s social isolation (NASEM 2020) without regard to the context of his/her social network such as having an isolated spouse. Study findings indicate a more holistic approach to understanding and addressing social isolation may be warranted. Married individuals—especially married men and dually-isolated spouses—may benefit from a couple-based approach to addressing social isolation. Prior research has found that individual and spousal assessment of self-rated health better predicts health status among married individuals than individual assessment alone (CITE). Research will be needed to establish the feasibility and efficacy of a contextual approach to understanding the health consequences of social isolation and the relative effectiveness of a couple-based strategy versus traditional, individual-focused strategies.

**Limitations**

A limitation of the study is that social isolation was assessed only at baseline and may have changed over time. Future studies should assess social isolation at multiple time points to determine the relative influence of baseline isolation on mortality. Still, although many social isolation-mortality associations attenuated with time in the current study, several remained statistically significant in the latter follow-up period. Another limitation is that the parent cohort study did not assess same-sex marriage nor cohabitation among unmarried partners, so findings may not be generalizable to all spouses or couples in a marriage-like relationship. Standard social isolation measures and methods may need to be updated to reflect a broader range of social relationships that are increasingly prevalent. Lastly, analyses did not account for possible divorce or remarriage as these data were not available.

AUTHORS:

* Mention here or in methods that this was a highly insured sample?
* Mention here or in methods that we didn’t account for a spouse dying during follow up because of an a priori conceptual rationale? Summarize time-varying analyses here or in methods? We might be underreporting associations in the second follow-up period because when a spouse dies, the surviving spouse becomes more isolated by definition (i.e., per the standard SNI measure).

**CONCLUSIONS**

Despite the established health-protective effect of marriage, this study of U.S adults found that social isolation is associated with a higher risk of death among opposite-sex spouses and that wives’ isolation affects mortality risk for both spouses. Assessment, and possibly intervention, of social isolation among married individuals should consider both spouses to better estimate and address social risk.

AUTHORS: Review tables on the following pages as well.

Table 1. Sex-Stratified Baseline Sample Characteristics by Social Isolation Status

|  |  |  |  |
| --- | --- | --- | --- |
|  | | **Isolated**  **(Scores 2/3)** | **Not Isolated**  **(Scores 0/1)** |
|  | | n (%) or mean (SD) | n (%) or mean (SD) |
| **MALES (n=143,663)** | |  |  |
| **Demographic Characteristics** | |  |  |
| Age (years)a | | 53.78 (8.92) | 55.15 (8.76) |
| Race/Ethnicity a | |  |  |
| Non-Hispanic White | 26,079 (95.3) | | 111,857 (96.2) |
| Non-Hispanic Black | | 594 (2.2) | 2,463 (2.1) |
| Hispanic | | 306 (1.1) | 769 (0.7) |
| Asian | | 241 (0.9) | 610 (0.5) |
| Other | | 153 (0.6) | 591 (0.5) |
| High school graduate or more a | | 23,411 (85.5) | 105,510 (90.7) |
| **Health Characteristics** | |  |  |
| Current smokera | | 7,604 (27.8) | 20,962 (18.0) |
| History of diabetesa | | 1,214 (4.4) | 4,550 (3.9) |
| Body Mass Index (kg/m2)c | | 26.05 (3.54) | 26.00 (3.26) |
| **Dyad Characteristics** | |  |  |
| Interracial Marriagea | | 657 (2.4) | 1,974 (1.7) |
| Residency Typea | |  |  |
| Urban | | 16,685 (61.0) | 67,421 (58.0) |
| Rural | | 2,680 (9.8) | 15,238 (13.1) |
| Mismatched | | 12 (0.0) | 46 (0.0) |
| Missing | | 7,996 (29.2) | 33,585 (28.9) |
| **FEMALES (n=143,663)** | |  |  |
| **Demographic Characteristics** | |  |  |
| Age (years)a | | 50.33 (9.03) | 52.13 (8.79) |
| Race/Ethnicitya | |  |  |
| Non-Hispanic White | | 14,397 (94.2) | 123,490 (96.2) |
| Non-Hispanic Black | | 323 (2.1) | 2,753 (2.1) |
| Hispanic | | 218 (1.4) | 929 (0.7) |
| Asian | | 240 (1.6) | 696 (0.5) |
| Other | | 106 (0.7) | 511 (0.4) |
| High school graduate or more a | | 13,665 (89.4) | 121,118 (94.3) |
| **Health Characteristics** | |  |  |
| Current smokera | | 4,469 (29.2) | 21,795 (17.0) |
| History of diabetesb | | 445 (2.9) | 3,184 (2.5) |
| Body Mass Index (kg/m2)c | | 24.20 (4.44) | 24.28 (4.20) |
| **Dyad Characteristics** | |  |  |
| Interracial Marriagea | | 450 (2.9) | 2,181(1.7) |
| Residency Typea | |  |  |
| Urban | | 9,339 (61.1) | 74,767 (58.2) |
| Rural | | 1,443 (9.4) | 16,475 (12.8) |
| Mismatched | | 8 (0.0) | 50 (0.0) |
| Missing | | 4,494 (29.4) | 37,087 (28.9) |

a p <0.001 b p <0.01 c p <0.05

Table 2. Social Isolation by Sex

|  |  |  |
| --- | --- | --- |
|  | **Males**  N=143,663  n (%) | **Females**  N=143,663  n (%) |
| **Social Isolation Score** |  |  |
| 0 | 64,004 (44.6) | 84,734 (59.0) |
| 1 | 52,286 (36.4) | 43,645 (30.4) |
| 2 | 22,052 (15.3) | 13,094 (9.1) |
| 3 | 5,321 (3.7) | 2,190 (1.5) |
| **Socially Isolated** |  |  |
| No (scores 0,1) | 116, 290 (80.9) | 128,379 (89.4) |
| Yes (scores 2,3) | 27,373 (19.1) | 15,284 (10.6) |

All P values <0.001

Matt: was p significant for the dichotomous variable as well (I’m guessing yes)?

Table 3. Associations of Social Isolation and Actor Mortality, by Follow-up Period

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **All-cause Mortality** | | **Cancer Mortality** | | **CVD Mortality** | |
|  | HR | 95% CI | HR | 95% CI | HR | 95% CI |
|  | **Follow-up period: 1982-1999** | | | | | |
|  |  |  |  |  |  |  |
| **Partner Isolation** |  |  |  |  |  |  |
| Not isolated | 1.00 | Ref. | 1.00 | Ref. | 1.00 | Ref. |
| Isolated | 1.05b | 1.02-1.08 | 1.06c | 1.01-1.11 | 1.02 | 0.97-1.07 |
| **Actor Isolation** |  |  |  |  |  |  |
| Not isolated | 1.00 | Ref. | 1.00 | Ref. | 1.00 | Ref. |
| Isolated | 1.15a | 1.12-1.18 | 1.10a | 1.05-1.15 | 1.13a | 1.08-1.18 |
| **Actor Sex** |  |  |  |  |  |  |
| Female | 1.00 | Ref. | 1.00 | Ref. | 1.00 | Ref. |
| Male | 1.71a | 1.68-1.75 | 1.44a | 1.39-1.50 | 2.10a | 2.02-2.18 |
|  | **Follow-up period: 2000-2016** | | | | | |
| **Partner Isolation** |  |  |  |  |  |  |
| Not isolated | 1.00 | Ref. | 1.00 | Ref. | 1.00 | Ref. |
| Isolated | 1.02 | 0.99-1.04 | 1.04c | 1.00-1.08 | 1.03 | 0.99-1.06 |
| **Actor Isolation** |  |  |  |  |  |  |
| Not isolated | 1.00 | Ref. | 1.00 | Ref. | 1.00 | Ref. |
| Isolated | 1.07a | 1.05-1.09 | 1.06b | 1.02-1.10 | 1.08a | 1.04-1.12 |
| **Actor Sex** |  |  |  |  |  |  |
| Female | 1.00 | Ref. | 1.00 | Ref. | 1.00 | Ref. |
| Male | 1.44a | 1.42-1.46 | 1.52a | 1.48-1.57 | 1.50a | 1.46-1.54 |

All models control for age, race/ethnicity, smoking status, history of diabetes, education level, and BMI.

a p <0.001 b p <0.01 c p <0.05

Table 4. Sex-Stratified Hazard Ratios for Associations of Spousal Isolation Concordance with Mortality, by Follow-up Period

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | **Males** | | | **Females** | |
|  | | HR | 95% CI |  | HR | 95% CI |
|  | **Follow-up period: 1982-1999** | | | | | |
| **All-Cause Mortality** | |  |  |  |  |  |
| Neither isolated | | 1.0000 | Ref. |  | 1.0000 | Ref. |
| Husband isolated | | 1.1500 a | 1.1123-1.1890 |  | 1.0180 | 0.9672-1.0714 |
| Wife isolated | | 1.1157 a | 1.0535-1.1816 |  | 1.1776 a | 1.0880-1.2745 |
| Both isolated | | 1.1999 a | 1.1486-1.2536 |  | 1.1748 a | 1.1033-1.2509 |
| **Cancer Mortality** | |  |  |  |  |  |
| Neither isolated | | 1.0000 | Ref. |  | 1.0000 | Ref. |
| Husband isolated | | 1.1285a | 1.0674-1.1932 |  | 1.0684 | 0.9908-1.1520 |
| Wife isolated | | 1.1053c | 1.0054-1.2152 |  | 1.0942 | 0.9679-1.2370 |
| Both isolated | | 1.1615a | 1.0797-1.2495 |  | 1.1247c | 1.0204-1.2400 |
| **CVD Mortality** | |  |  |  |  |  |
| Neither isolated | | 1.0000 | Ref. |  | 1.0000 | Ref. |
| Husband isolated | | 1.1078a | 1.0500-1.1689 |  | 0.9637 | 0.8762-1.0598 |
| Wife isolated | | 1.0925 | 0.9961-1.1982 |  | 1.2196b | 1.0583-1.4056 |
| Both isolated | | 1.1300a | 1.0521-1.2137 |  | 1.1732b | 1.0481-1.3132 |
|  | **Follow-up period: 2000-2016** | | | | | |
| **All-Cause Mortality** | |  |  |  |  |  |
| Neither isolated | | 1.0000 | Ref. |  | 1.0000 | Ref. |
| Husband isolated | | 1.0762a | 1.0473-1.1059 |  | 1.0190 | 0.9901-1.0489 |
| Wife isolated | | 1.0314 | 0.9857-1.0792 |  | 1.0544c | 1.0048-1.1065 |
| Both isolated | | 1.0701 a | 1.0316-1.1101 |  | 1.1150a | 1.0732-1.1584 |
| **Cancer Mortality** | |  |  |  |  |  |
| Neither isolated | | 1.0000 | Ref. |  | 1.0000 | Ref. |
| Husband isolated | | 1.0672c | 1.0143-1.1229 |  | 1.0568 | 0.9982-1.1188 |
| Wife isolated | | 1.0408 | 0.9572-1.1318 |  | 1.0807 | 0.9843-1.1865 |
| Both isolated | | 1.0545 | 0.9847-1.1292 |  | 1.1326b | 1.0509-1.2206 |
| **CVD Mortality** | |  |  |  |  |  |
| Neither isolated | | 1.0000 | Ref. |  | 1.0000 | Ref. |
| Husband isolated | | 1.0578c | 1.0086-1.1093 |  | 1.0110 | 0.9608-1.0639 |
| Wife isolated | | 1.0066 | 0.9294-1.0902 |  | 1.0416 | 0.9551-1.1359 |
| Both isolated | | 1.1203a | 1.0525-1.1925 |  | 1.1502a | 1.0760-1.2295 |

All models control for age, smoking status, history of diabetes, education level, race, and BMI.

a p <0.001 b p <0.01 c p <0.05

Matt: Can you double-check whether these models controlled for race/ethnicity? They should, but I want to confirm.

**REFERENCES**

tbd based on final version