American Journal of Epidemiology

Vol. 188, No. 1
DOI: 10.1093/aje/kwy231
Advance Access publication:
October 16, 2018

Original Contribution

Social Isolation and Mortality in US Black and White Men and Women

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Initially submitted November 7, 2017; accepted for publication September 24, 2018.

Social isolation is associated with higher mortality in studies comprising mostly white adults, yet associations among black adults are unclear. In this prospective cohort study, we evaluated whether associations of social isolation with all-cause, cardiovascular disease, and cancer mortality differed by race and sex. Adults enrolled in Cancer Prevention Study II in 1982/1983 were followed for mortality through 2012 ($n = 580{,}182$). Sex- and race-specific multivariable-adjusted hazard ratios and 95% confidence intervals were estimated for associations of a 5-point social isolation score with risk of death. Social isolation was associated with all-cause mortality in all subgroups (P for trend ≤ 0.005); for the most isolated versus the least isolated, the hazard ratios were 2.34 (95% confidence interval (CI): 1.58, 3.46) and 1.60 (95% CI: 1.41, 1.82) among black men and white men, respectively (P for interaction = 0.40) and 2.13 (95% CI: 1.44, 3.15) and 1.84 (95% CI: 1.68, 2.01) among black women and white women, respectively (P for interaction = 0.89). The association did not differ between black men and black women (P for interaction = 0.33) but was slightly stronger in white women than in white men (P for interaction = 0.01). Social isolation was associated with cardiovascular disease mortality in each subgroup (P for trend < 0.03) but with cancer mortality only among whites (P for trend < 0.0001). Subgroup differences in the influence of specific social isolation components were identified. Identifying and intervening with socially isolated adults could improve health outcomes.

cancer; Cancer Prevention Study II; cardiovascular disease; cohort studies; health disparities; mortality; race; social isolation

Abbreviations: CPS-II, Cancer Prevention Study II; CVD, cardiovascular disease; HR, hazard ratio; ICD-9, *International Classification of Diseases, Ninth Revision*; ICD-10, *International Classification of Diseases, Tenth Revision*.

Social isolation—a measure of an individual's (limited) social contact and networks—is detrimental to health and well-being (1–4). Berkman and Syme (5) developed the Social Network Index, a summary measure of social isolation derived from several components: marital status, participation in church groups and other groups, and number and frequency of contact with close friends/relatives. In age-adjusted analyses, they found that men and women who were the most isolated had 2.3-fold and 2.8-fold higher risks of premature mortality, respectively, than the least isolated (5). Dozens of subsequent studies using various social isolation measures have examined associations with overall mortality, with weighted mean effect sizes between 1.29 and 1.83 (4).

The prevalence of social isolation differs across population subgroups (3, 6), yet evidence on its association with mortality across subgroups is limited. Research has found black-white differences in the health-protective associations of religious involvement (with protective associations being stronger among blacks) (7–9) and number of social contacts (with protective associations being stronger among whites) (9). However, the extent to which these racial differences persist using a measure of social isolation (i.e., one that considers both religious participation and interpersonal relationships) is unknown. Additionally, findings from research examining sex differences in the association between social isolation and mortality have been inconsistent. Some studies, comprising mostly white adults, have suggested that the association between social isolation and all-cause mortality may be similar for women and men (10, 11), although other studies have suggested that social isolation is more deleterious for men (1, 12). Many studies examining sex differences

have been hindered by limited statistical power (13–16), and the literature lacks robust evidence on the association between social isolation and mortality by race *and* sex. Liu (6) studied 9,246 older adults and found the association between social isolation and all-cause mortality to be weakest among white men and strongest among black women. Schoenbach et al. (14) examined social isolation and all-cause mortality in 2,059 adults and found an association only among white men; the association became nonsignificant after adjustment for potential confounders.

The American Cancer Society's Cancer Prevention Study II (CPS-II) cohort provides an opportunity to examine associations between social isolation and mortality in race-sex subgroups (i.e., black women, black men, white women, and white men) because of its large sample size, comprehensive risk factor assessment, and long-term follow-up for mortality. Using CPS-II data, we compared associations of social isolation with all-cause, cardiovascular disease (CVD), and cancer mortality among sex-race subgroups. Such findings can inform unanswered questions about the role of social isolation in mortality in these subgroups and might be useful in identifying and intervening with patients who are vulnerable to premature death.

METHODS

The Cancer Prevention Study II cohort

Detailed information on CPS-II recruitment methods was reported previously (17). Briefly, in 1982/1983, nearly 1.2 million (n = 1,185,106) adults aged 30 years or older were enrolled by American Cancer Society volunteers in all 50 US states, the District of Columbia, and Puerto Rico. Participants completed a mailed, 4-page self-administered questionnaire on demographic, medical, occupational, anthropometric, lifestyle, and behavioral factors, including components of social isolation. The CPS-II protocol was approved by the Institutional Review Board of Emory University (Atlanta, Georgia).

To eliminate possible bias due to reverse causality, CPS-II participants who, in 1982/1983, reported a personal history of cancer, heart disease, stroke, or chronic obstructive pulmonary disease (n = 233,312) were excluded from the analysis. We also excluded participants who were missing information on a social isolation component (n = 217,962), had nonnumerical information for a social isolation component (e.g., "very few") (n = 108,882), reported race other than black or white (n = 12,994), or provided incomplete or uninterpretable information on smoking (n = 30,149). Also excluded were men over age 90 years (≥90 years) and women over age 95 years (≥95 years) at baseline (n = 873), because a small percentage of deaths at very advanced ages are missed by National Death Index linkage, potentially resulting in significant misclassification of vital status (18). After accounting for participants who revoked participation or were lost to follow-up (n = 752), 580,182 participants (49%) were included in the analyses.

Assessment and scoring components of social isolation

The CPS-II baseline questionnaire queried participants on marital status, frequency of church/temple attendance and club meetings/group activities, and number of close friends/relatives. Consistent with other research employing Social Network Index components (15, 16), we weighted each component equally with a score of 0 (least isolated) or 1 (most isolated). Participants who reported being married were assigned a score of 0; those who reported being single, separated, divorced, or widowed were assigned a score of 1. Participants who reported attending church/temple (hereafter, "religious services") at least once per month were assigned a score of 0; participants who attended religious services less frequently or not at all were assigned a score of 1. Participants who reported attending club meetings/group activities at least once per month were assigned a score of 0; participants who attended club meetings/group activities less frequently or not at all were assigned a score of 1. The average number of close friends/relatives reported by CPS-II participants was high (mean = 28); a score of 0 was assigned to those who reported having 7 or more close friends or relatives (which represented approximately 87% of CPS-II participants included for analysis); participants who reported 6 or fewer close friends or relatives were assigned a score of 1. This approach is similar to that used in other studies in which this variable was coded on the basis of frequency distributions (6, 16). The 5-point social isolation score (exposure) was the sum of scores for the 4 individual components and ranged from 0 for least isolated to 4 for most isolated.

Mortality follow-up

Vital status was determined using 2 approaches. Through 1988, American Cancer Society volunteers made personal inquiries to determine participants' vital status and the dates and places of deaths. Death certificates were obtained to verify reported deaths and to assess information on the cause of death. At completion of the 1988 follow-up, vital status was known for 98.2% of the cohort. Subsequently, linkage to the National Death Index was used to identify deaths from September 1988 through December 2012 and deaths among the 21,704 participants lost to follow-up between 1982 and 1988. Cause of death is known for more than 99% of all known deaths.

The underlying cause of death was coded in accordance with the *International Classification of Diseases, Ninth Revision* (ICD-9) and the *International Classification of Diseases, Tenth Revision* (ICD-10) (19, 20). For this analysis, primary outcomes were all-cause mortality (ICD-9 codes 001–999, V01–V99, and E000–E999; ICD-10 codes A00–Z99), CVD mortality (ICD-9 codes 390–459 and 798; ICD-10 codes I00–I99 and R96), and cancer mortality (ICD-9 codes 140–239; ICD-10 codes C00–C97 and D00–D49).

Statistical analysis

Person-years of follow-up were computed as the amount 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, 2012 (whichever came first).

We computed hazard ratios and 95% confidence intervals for risk of death from all causes for persons with social isolation scores of 1–4 compared with those with scores of 0 (least isolated), using Cox proportional hazards regression (21). Because of limited statistical power for analyses of CVD and cancer mortality in black men and women, the social isolation scores of 3 and 4 were combined for all race-sex subgroups for these

mortality outcomes. All models adjusted for race and single year of age using the stratified Cox procedure. Multivariable-adjusted models additionally included dummy variables, including dummy-coding of missing data for variables with missing data. Dummy variables were created for educational level (less than high school, high school, some college, college graduation, or missing), body mass index (weight (kg) divided by squared height (m^2); <18.5, 18.5–24.9, 25–29.9, ≥30.0, or missing), smoking history (never smoker, current smoker (<20 cigarettes/day, ≥20 cigarettes/day, or unknown), former smoker (<10 years since quitting, 10–19.9 years since quitting, ≥20 years since quitting, or missing), or cigar/pipe smoker), diabetes mellitus status (no, yes), and sex.

Race-/sex-specific mean values and distributions of sociodemographic and other factors across categories of social isolation score were examined to assess potential confounding. Adjustment for alcohol intake, aspirin use, employment status, vegetable intake, red and processed meat intake, family history of cancer, physical activity, and postmenopausal hormone use among women had a negligible influence on risk; therefore, these factors were not included in the models. The associations of individual components of the social isolation score (mutually adjusted) with all-cause mortality were also assessed. As an additional metric to evaluate the linear trend across the entire distribution of the social isolation score, *P* values for trends were determined using a continuous variable for the score.

Because social isolation was assessed only at baseline and may have changed during follow-up, we compared associations between social isolation score and risk of all-cause mortality during the first (1982–1997) and second (1998–2012) 15 years of follow-up, among all race-sex subgroups combined. We computed *P* values for multiplicative interactions using likelihood ratio tests that compared models with and without cross-product terms for social isolation score and each of the 2 follow-up periods.

Differences in associations between social isolation and mortality risk by sex and by race were assessed using likelihood ratio tests that compared models with and without cross-product terms for social isolation score (continuous) or individual components (dichotomous) and sex or race. Because smoking is a major cause of death that is also associated with social isolation, in sensitivity analyses we compared the associations between social isolation score and mortality risk among never, former, and current smokers, using likelihood ratio tests comparing models with and without cross-product terms for social isolation score and smoking status. All analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, North Carolina), and all tests of significance were 2-sided, with α set at $P < 0.05$.

RESULTS

Social isolation exposure

In our study population, black women were the most likely to be unmarried; black men and black women were the most likely to have few close friends/relatives; white men were the most likely to attend religious services infrequently; and black men and white men were the most likely to participate in clubs/groups infrequently (Table 1). Overall, race seemed to be a stronger predictor of social isolation score than sex, as both white men and white women were more likely to be in the least isolated category than black men and black women. In all race-sex subgroups, the proportion of current smokers increased and the proportion of persons with at least a high school education decreased with increasing social isolation (Table 2).

Table 1. Exposure to Social Isolation (%), by Race and Sex, in the Cancer Prevention Study II Cohort, United States, 1982–2012

Exposure	Race-Sex Subgroup			
	Black Men (*n* = 7,348)	White Men (*n* = 238,206)	Black Women (*n* = 13,320)	White Women (*n* = 321,308)
Social isolation component[a]				
Not married	15.2	5.1	38.7	19.8
<7 Close friends/relatives	27.3	20.5	24.6	15.4
Religious service attendance less than once per month	18.5	25.6	7.1	17.1
Club/group participation less than once per month	39.1	37.1	30.8	26.0
Social isolation score[a,b]				
0 (least isolated)	36.1	40.7	34.3	45.8
1	36.6	36.4	38.1	35.3
2	19.4	17.3	20.4	14.5
3	6.8	5.1	6.3	3.8
4 (most isolated)	1.1	0.5	0.8	0.6

[a] All *P* values < 0.0001.
[b] Percentages may not sum to 100 because of rounding.

Table 2. Baseline Characteristics of Participants According to Social Isolation Score, by Race and Sex, in the Cancer Prevention Study II Cohort, United States, 1982–2012

Race-Sex Subgroup and Characteristic	Social Isolation Score									
	0 (Least Isolated)		1		2		3		4 (Most Isolated)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Black men										
No. of men	2,653	36.1	2,689	36.6	1,429	19.5	498	6.8	79	1.1
Age, years[a]	55.4 (9.9)		54.5 (10.9)		52.9 (11.5)		51.4 (12.1)		47.6 (12.1)	
High school education or more[b]	2,201	83.0	1,900	70.7	953	66.7	305	61.2	47	59.5
Current smoker[b]	806	30.4	951	35.4	622	43.6	271	54.4	54	68.4
History of diabetes	260	9.8	238	8.9	131	9.2	40	8.0	8	10.1
Body mass index[a,c]	26.7 (3.8)		26.6 (3.9)		26.5 (4.0)		26.4 (4.7)		24.1 (3.7)	
White men										
No. of men	96,902	40.7	86,786	36.4	41,146	17.3	12,196	5.1	1,176	0.5
Age, years[a]	56.2 (9.0)		55.6 (9.5)		54.4 (10.0)		52.8 (10.8)		49.3 (13.6)	
High school education or more[b]	89,544	92.4	76,129	87.7	35,393	86.0	10,387	85.2	1,023	87.0
Current smoker[b]	17,576	18.2	20,396	23.5	12,295	29.9	4,346	35.7	467	39.7
History of diabetes[b]	3,906	4.0	3,715	4.3	1,819	4.4	561	4.6	43	3.7
Body mass index[a]	26.0 (3.2)		26.0 (3.3)		26.0 (3.5)		25.9 (3.7)		25.0 (3.9)	
Black women										
No. of women	4,574	34.3	5,079	38.1	2,722	20.4	833	6.3	112	0.8
Age, years[a]	52.6 (9.6)		53.4 (11.7)		53.8 (12.8)		52.7 (14.5)		50.9 (15.1)	
High school education or more[b]	3,962	86.6	3,993	78.6	1,843	67.7	508	61.0	75	67.0
Current smoker[b]	1,116	24.4	1,367	26.9	856	31.4	291	34.9	52	46.5
History of diabetes	332	7.3	411	8.1	216	7.9	73	8.8	11	9.8
Body mass index[a]	26.7 (4.8)		27.3 (5.4)		27.1 (5.6)		27.1 (6.0)		27.2 (7.0)	
White women										
No. of women	147,035	45.8	113,524	35.3	46,458	14.5	12,365	3.9	1,926	0.6
Age, years[a]	53.7 (9.1)		55.3 (10.7)		55.2 (11.7)		55.4 (13.1)		56.4 (15.1)	
High school education or more[b]	138,458	94.2	101,348	89.3	39,720	85.5	10,112	81.8	1,497	77.7
Current smoker[b]	22,680	15.4	23,410	20.7	12,885	27.7	4,272	34.6	798	41.4
History of diabetes[b]	3,806	2.6	3,593	3.2	1,691	3.6	544	4.4	96	5.0
Body mass index[a]	24.4 (4.2)		24.4 (4.4)		24.5 (4.6)		24.4 (4.8)		24.6 (5.4)	

[a] Values are expressed as mean (standard deviation).
[b] $P < 0.001$.
[c] Weight (kg)/height $(m)^2$.

Social isolation score and all-cause mortality

In the full sample, a statistically significant, positive dose-response relationship was found between social isolation and all-cause mortality risk over the 30-year follow-up period (P for trend < 0.0001; see Web Table 1, available at https://academic.oup.com/aje). This association was stronger during the first 15 years of follow-up than during the second 15 years (e.g., for the most isolated vs. the least isolated, hazard ratios were 1.76 and 1.22, respectively; P for difference $<$ 0.0001). Because this attenuation over time may have been due to increasing misclassification of social isolation during the later years of follow-up, all other analyses were based on the first 15-year follow-up period. There was no difference in association between social isolation and all-cause mortality by smoking status (Web Table 2).

In race-sex subgroup analyses, statistically significant positive associations between social isolation score and all-cause mortality were observed in each subgroup (P for trend ≤ 0.005) (Web Table 3). Within each sex group, there was no evidence of interaction by race (in men, P for interaction $= 0.40$; in women, P for interaction $= 0.89$). However, among whites, the hazard ratio for the most isolated persons versus the least isolated was higher among women (hazard ratio (HR) $= 1.84$) than among men (HR $= 1.60$) (P for interaction $= 0.01$), whereas among blacks, the hazard ratio for the most isolated persons compared with the least isolated did not differ by sex (P for interaction $= 0.33$).

Table 3. Association of Components of a Social Isolation Score With Mortality in the Cancer Prevention Study II Cohort, United States, 1982–1997[a]

Isolation Score Component	No. of Persons	No. of Person-Years	All-Cause Mortality			CVD Mortality			Cancer Mortality		
			No. of Cases	HR	95% CI	No. of Cases	HR	95% CI	No. of Cases	HR	95% CI
Marital status											
Married	498,227	7,208,472	65,903	1	Referent	25,281	1	Referent	24,754	1	Referent
Not married	81,955	1,128,177	17,895	1.17	1.15, 1.19	8,084	1.25	1.22, 1.29	4,966	1.04	1.01, 1.08
No. of close friends/relatives											
≥7	476,649	6,846,893	69,470	1	Referent	27,828	1	Referent	24,671	1	Referent
<7	103,533	1,489,756	14,328	1.05	1.03, 1.06	5,537	1.04	1.01, 1.07	5,049	1.02	0.99, 1.05
Club/group participation, no. of times per month											
≥1	401,430	5,817,289	52,073	1	Referent	20,384	1	Referent	19,007	1	Referent
<1	178,752	2,519,359	31,725	1.13	1.12, 1.15	12,981	1.15	1.13, 1.18	10,713	1.08	1.05, 1.11
Religious service attendance, no. of times per month											
≥1	461,986	6,652,783	64,967	1	Referent	26,277	1	Referent	22,794	1	Referent
<1	118,196	1,683,866	18,831	1.09	1.07, 1.11	7,088	1.05	1.02, 1.08	6,926	1.09	1.06, 1.12

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio.

[a] The models stratified the data on age (in single years) and race, and results were adjusted for sex, smoking status, education, body mass index, history of diabetes, and all other social isolation components.

Social isolation score and cause-specific mortality

Social isolation score was positively associated with CVD mortality in all subgroups (Web Table 3). The strength of this association did not differ between black women and white women (P for interaction = 0.75), between black men and black women (P for interaction = 0.39), or between black men and white men (P for interaction = 0.73). However, the association was stronger among white women than among white men (P for interaction < 0.0001).

Although there was a positive association between social isolation score and cancer mortality among white men and white women (P for trend < 0.0001), this association did not differ by sex (P for interaction = 0.32). There was no association between social isolation score and cancer mortality among black men (P for trend = 0.32) or black women (P for trend = 0.87).

Social isolation components and mortality

Overall, each component of the social isolation score was associated with all-cause mortality and CVD mortality (Table 3). The hazard ratios for being unmarried and for infrequently participating in clubs/groups, respectively, were higher than those for infrequently attending religious services or having fewer than 7 close friends/relatives. Having fewer than 7 close friends/relatives was not associated with cancer mortality, whereas each of the other 3 components of the social isolation score was associated with a statistically significantly higher cancer mortality risk.

Analyses of each social isolation component with all-cause mortality by sex and race (Figure 1) indicated that among men, being unmarried was associated with a statistically significantly higher risk of mortality; this association did not differ by race (P for interaction = 0.22). Being unmarried was more strongly associated with mortality among men than among women in both races (P for interaction < 0.01). Other social isolation components showed statistically significant positive hazard ratios for all-cause mortality among white men but not black men, yet the P values for interaction provided little support for differences in associations by race (P for interaction ≥ 0.13). Each component was statistically significantly associated with all-cause mortality among white women, and all components except number of close friends/relatives were associated with all-cause mortality among black women. Black women who attended religious services less than once per month (compared with more often) had a 32% higher risk of mortality, whereas white women who infrequently attended services had an 11% higher risk (P for interaction = 0.04). However, among women, the hazard ratios for the other 3 components did not appear to differ by race (P for interaction ≥ 0.50). Among blacks, the relationship between religious service attendance and all-cause mortality differed between black women (HR = 1.32, 95% confidence interval: 1.12, 1.55) and black men (HR = 0.98, 95% confidence interval: 0.86, 1.11) (P for interaction = 0.006).

DISCUSSION

To our knowledge, this was the largest study to date on associations between social isolation and mortality in multiple race-sex subgroups in a nationwide US cohort. Social isolation was positively associated with all-cause and CVD mortality in the 4 race-sex subgroups examined and with cancer mortality in white men and women only. Each social isolation

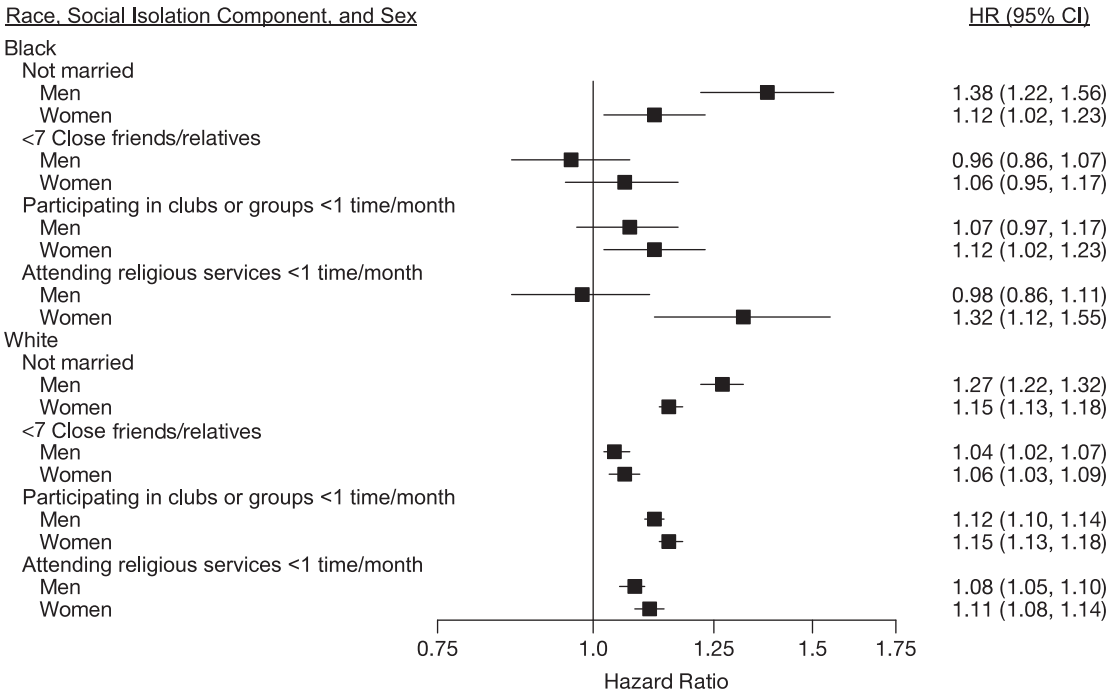

Figure 1. Association of components of a social isolation score with all-cause mortality, by race and sex, in the Cancer Prevention Study II cohort, United States, 1982–1997. The models stratified the data on age (in single years), and results were adjusted for smoking status, education, body mass index, history of diabetes, and all other social isolation components. CI, confidence interval; HR, hazard ratio.

component was associated with all-cause and CVD mortality, and all but one (having fewer close friends/relatives) were associated with cancer mortality.

Similarly to previous studies (5, 6), current findings indicate that a composite measure of social isolation is a robust predictor of mortality risk among men, women, blacks, and whites. Compared with the least isolated, the most socially isolated black men and women had a more than 2-fold higher risk of death from any cause, and white men and women had 60% and 84% greater risks of death, respectively. Two other studies of social isolation and mortality reported findings for both blacks and whites. Schoenbach et al. (14) found no associations in race-sex subgroups after controlling for potential confounders, although that study included 735 blacks and therefore power was limited. Our study's general pattern of results mirrors findings by Liu (6), except that risk estimates from that study were smaller in magnitude (hazard ratios of 1.25–1.82 vs. 1.60–2.34 in the current study).

Social isolation was associated with CVD mortality in each race-sex subgroup examined, with a 29% higher risk of CVD death for white men and an approximately 50% higher risk for each of the other 3 race-sex subgroups. Comparable studies examining race-sex subgroup differences are lacking. In the only other study that examined this association by race/ethnicity, there was an elevated risk of CVD mortality among the most socially isolated blacks (HR = 2.01) and whites (HR = 1.71) (22). In the few studies that examined social isolation and CVD mortality by sex only (15) or among men only (13, 23, 24), none found an association. Our study's conflicting findings in this regard may reflect its longer follow-up period and/or larger sample.

Results indicate 25% and 26% higher risks of death from cancer for the most socially isolated white men and white women (compared with the least isolated), respectively, but no association among black men or black women. With one exception (13), other studies have found no association between social isolation and cancer mortality among men (16, 23, 24). Reynolds and Kaplan (16) reported a 2.2 times' higher risk of cancer mortality among the most socially isolated women, but not among men. In a study of older adults, Liu and Newschaffer (22) reported a higher risk of death from cancer for the most socially isolated blacks (HR = 2.56) and whites (HR = 1.40). The present study's conflicting results may reflect subgroup differences in health-care utilization, clinical cancer characteristics, or the relative influence of social isolation compared with other important cancer mortality risk factors. Our study's findings on cancer mortality and social isolation by race-sex subgroup underscore the need to elucidate this seemingly complex relationship. Research on site-specific cancer mortality may provide additional insights.

Understanding associations of social isolation components with mortality can identify dimensions of isolation that may exert more or less influence on health. Lack of interpersonal connections seems particularly detrimental. Being unmarried was associated with all-cause mortality—particularly for men—and with CVD and cancer mortality, consistent with literature indicating that unmarried persons—especially men—have poorer health and greater mortality risk than married persons (25). Berkman et al. (13) found that approximately half of the risk associated with social isolation was due to marital status for men, yet (contrary to our findings) marital status was even more important for women. Findings indicate that having relatively fewer close

friends/relatives also is important, although this component was not associated with cancer mortality overall or with all-cause mortality among black men or black women. Lacking involvement in groups seems to be detrimental as well. Our study found regular club/group participation and religious service attendance to predict all-cause, CVD, and cancer mortality risk. Further, findings indicated that black women who attend religious services infrequently are at greater risk of all-cause mortality compared with other race-sex subgroups. Evidence suggests a positive association between African Americans' religious participation and health (e.g., health behavior, health-care practices, coping/mental health, social support) (8, 26–29). Research is needed to examine why different types of social linkages have different associations with mortality within population subgroups.

Addressing social isolation may facilitate improved health outcomes. In a recent meta-analytical review, Holt-Lunstad et al. (4) identified social isolation as an independent risk factor for death on par with well-established mortality risk factors such as physical inactivity, obesity, and lack of access to health care. Notably, Liu (6) found that when combined with having diabetes mellitus, the mortality risk for the least socially connected black women and men was 3 times higher than that for well-connected black women and men. Although research confirming mechanisms is needed, social isolation is hypothesized to influence health via multiple pathways, including psychological (e.g., depression, stress), behavioral (e.g., sleep), interpersonal (e.g., instrumental social support), medical (e.g., adherence), physiological (e.g., neuroendocrine functioning), and/or genetic (e.g., gene expression) routes (30–32). Persistent challenges in intervening on modifiable clinical risk factors such as obesity make approaches based on social isolation promising if efficacy can be established. In addition to the relatively low complexity of such approaches (e.g., identification and referral), another benefit of addressing social isolation is the potential to influence multiple risk factors, as it is associated with hypertension, markers of inflammation, physical inactivity, smoking, and other health-risk behaviors (12, 30, 33). In the era of precision medicine, multiple influences on health—including social factors—are expected to be increasingly considered in clinical care, and addressing social isolation is aligned with this more holistic approach.

Major strengths of this study were its large sample (which overcame the power limitations of previous studies), its prospective design, and the availability of data on several components of social isolation. However, the study was not without limitations. Social integration may vary with time, and recall of activities/interactions is subject to retrospective bias (34). In our study, data on social isolation were not updated over time, and self-reported data are subject to misclassification, although there is no reason to expect that inaccurate reporting of social isolation information would be strongly related to future mortality risk. Additionally, unlike the original Social Network Index (5), data were not collected on the frequency of contact with close relatives/friends. Further, the marital status component of the social isolation measure did not account for unmarried persons who were living with a significant other. Lastly, weighting each social isolation component equally in the social isolation score might not precisely reflect the relative importance of certain components (e.g., personal relationships vs. group participation). However, weighting is not advised unless a strong, a priori conceptual rationale exists (34), and our intent for this study was to utilize a parsimonious social isolation measure.

Recent literature has called for more epidemiologic research on social isolation and health, particularly due to a lack of robust evidence on the association of social isolation with cancer outcomes (35) and the growing use of technology to "connect" socially (36). Seeking to help fill existing research gaps, this study found that social isolation was associated with higher mortality risk for all of the race-sex subgroups studied. These findings lend support to the growing assertion (3, 31, 37, 38) that attending to social as well as clinical risk factors holds promise for reducing mortality in the United States. Research is needed to identify effective social isolation interventions that can be adopted in clinical or other settings.

ACKNOWLEDGMENTS

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The American Cancer Society funded all aspects of data collection and analysis. As a Building Interdisciplinary Research Careers in Women's Health scholar, K.S.E.'s contribution was supported in part by the Office of Research on Women's Health, National Institutes of Health (grant K12 DA035150).

We express sincere appreciation to all Cancer Prevention Study II participants.

Conflict of interest: none declared.

REFERENCES

1. House JS, Landis KR, Umberson D. Social relationships and health. *Science*. 1988;241(4865):540–545.
2. Umberson D, Montez JK. Social relationships and health: a flashpoint for health policy. *J Health Soc Behav*. 2010; 51(1 suppl):S54–S66.
3. Pantell M, Rehkopf D, Jutte D, et al. Social isolation: a predictor of mortality comparable to traditional clinical risk factors. *Am J Public Health*. 2013;103(11):2056–2062.
4. Holt-Lunstad J, Smith TB, Baker M, et al. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect Psychol Sci*. 2015;10(2):227–237.
5. Berkman LF, Syme SL. Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. *Am J Epidemiol*. 1979;109(2):186–204.
6. Liu L. Social connections, diabetes mellitus, and risk of mortality among white and African-American adults aged 70 and older: an eight-year follow-up study. *Ann Epidemiol*. 2011; 21(1):26–33.

7. Krause N. Church-based social support and health in old age: exploring variations by race. *J Gerontol B Psychol Sci Soc Sci*. 2002;57(6):S332–S347.
8. Reese AM, Thorpe RJ, Jr., Bell CN, et al. The effect of religious service attendance on race differences in depression: findings from the EHDIC-SWB Study. *J Urban Health*. 2012; 89(3):510–518.
9. Assari S. Whites but not blacks gain life expectancy from social contacts. *Behav Sci (Basel)*. 2017;7(4):pii:E68.
10. Barger SD. Social integration, social support and mortality in the US National Health Interview Survey. *Psychosom Med*. 2013;75(5):510–517.
11. Steptoe A, Shankar A, Demakakos P, et al. Social isolation, loneliness, and all-cause mortality in older men and women. *Proc Natl Acad Sci U S A*. 2013;110(15):5797–5801.
12. Yang YC, McClintock MK, Kozloski M, et al. Social isolation and adult mortality: the role of chronic inflammation and sex differences. *J Health Soc Behav*. 2013;54(2):183–203.
13. Berkman LF, Melchior M, Chastang JF, et al. Social integration and mortality: a prospective study of French employees of Electricity of France-Gas of France: the GAZEL cohort. *Am J Epidemiol*. 2004;159(2):167–174.
14. Schoenbach VJ, Kaplan BH, Fredman L, et al. Social ties and mortality in Evans County, Georgia. *Am J Epidemiol*. 1986; 123(4):577–591.
15. Kaplan GA, Salonen JT, Cohen RD, et al. Social connections and mortality from all causes and from cardiovascular disease: prospective evidence from eastern Finland. *Am J Epidemiol*. 1988;128(2):370–380.
16. Reynolds P, Kaplan GA. Social connections and risk for cancer: prospective evidence from the Alameda County Study. *Behav Med*. 1990;16(3):101–110.
17. Calle EE, Rodriguez C, Jacobs EJ, et al. The American Cancer Society Cancer Prevention Study II Nutrition Cohort: rationale, study design, and baseline characteristics. *Cancer*. 2002;94(2): 500–511.
18. Calle EE, Terrell DD. Utility of the National Death Index for ascertainment of mortality among Cancer Prevention Study II participants. *Am J Epidemiol*. 1993;137(2):235–241.
19. World Health Organization. *International Classification of Diseases, Ninth Revision*. Geneva, Switzerland: World Health Organization; 1977.
20. World Health Organization. *International Classification of Diseases, Tenth Revision*. Geneva, Switzerland: World Health Organization; 1992.
21. Cox DR. Regression models and life-tables (with discussion). *J Royal Stat Soc Series B Stat Methodol*. 1972;34(2):187–220.
22. Liu L, Newschaffer CJ. Impact of social connections on risk of heart disease, cancer, and all-cause mortality among elderly Americans: findings from the Second Longitudinal Study of Aging (LSOA II). *Arch Gerontol Geriatr*. 2011;53(2): 168–173.
23. Kawachi I, Colditz GA, Ascherio A, et al. A prospective study of social networks in relation to total mortality and cardiovascular disease in men in the USA. *J Epidemiol Community Health*. 1996;50(3):245–251.
24. Eng PM, Rimm EB, Fitzmaurice G, et al. 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*. 2002;155(8):700–709.
25. Robards J, Evandrou M, Falkingham J, et al. Marital status, health and mortality. *Maturitas*. 2012;73(4):295–299.
26. Felix Aaron K, Levine D, Burstin HR. African American church participation and health care practices. *J Gen Intern Med*. 2003;18(11):908–913.
27. van Olphen J, Schulz A, Israel B, et al. Religious involvement, social support, and health among African-American women on the east side of Detroit. *J Gen Intern Med*. 2003;18(7):549–557.
28. Holt CL, Clark EM, Debnam KJ, et al. Religion and health in African Americans: the role of religious coping. *Am J Health Behav*. 2014;38(2):190–199.
29. Fothergill KE, Ensminger ME, Robertson J, et al. Effects of social integration on health: a prospective study of community engagement among African American women. *Soc Sci Med*. 2011;72(2):291–298.
30. Yang YC, Boen C, Gerken K, et al. Social relationships and physiological determinants of longevity across the human life span. *Proc Natl Acad Sci U S A*. 2016;113(3):578–583.
31. Holt-Lunstad J, Smith TB. Loneliness and social isolation as risk factors for CVD: implications for evidence-based patient care and scientific inquiry. *Heart*. 2016;102(13):987–989.
32. House JS. Social isolation kills, but how and why? *Psychosom Med*. 2001;63(2):273–274.
33. Shankar A, McMunn A, Banks J, et al. Loneliness, social isolation, and behavioral and biological health indicators in older adults. *Health Psychol*. 2011;30(4):377–385.
34. Brissette I, Cohen S, Seeman T. Measuring social integration and social networks. In: Cohen S, Underwood LG, Gottlieb BH, eds. *Social Support Measurements and Interventions: A Guide for Social and Health Scientists*. New York, NY: Oxford University Press; 2000:53–85.
35. Leigh-Hunt N, Bagguley D, Bash K, et al. An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health*. 2017;152:157–171.
36. Aiello AE. Invited commentary: evolution of social networks, health, and the role of epidemiology. *Am J Epidemiol*. 2017; 185(11):1089–1092.
37. Alcaraz KI, Sly J, Ashing K, et al. The ConNECT framework: a model for advancing behavioral medicine science and practice to foster health equity. *J Behav Med*. 2017;40(1): 23–38.
38. Klinenberg E. Social isolation, loneliness, and living alone: identifying the risks for public health. *Am J Public Health*. 2016;106(5):786–787.