The prospective association of social integration with lifespan and exceptional longevity in women

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Abstract

Objectives: Although stronger social relationships have been associated with reduced mortality risk in prior research, their associations with favorable health outcomes are understudied. We evaluated whether higher social integration levels were associated with longer lifespan and greater likelihood of achieving exceptional longevity.

Method: Women from the Nurses' Health Study completed the Berkman-Syme Social Network Index in 1992 (N=72,322; average age=58.80 years), and were followed through 2014 with biennial questionnaires. Deaths were ascertained from participants' families, postal authorities, and death registries. Accelerated failure time models adjusting for relevant covariates estimated percent changes in lifespan associated with social integration levels; logistic regressions evaluated likelihood of surviving to age 85 or older among women who could reach that age during follow-up (N=16,818).

Results: After controlling for baseline demographics and chronic diseases, socially integrated versus isolated women had 10% (95%Confidence Interval [CI]=8.80-11.42) longer lifespan and 41% (95%CI=1.28-1.54) higher odds of surviving to age 85 years. All findings remained statistically significant after further adjusting for health behaviors and depression.

Discussion: Better social integration is related to longer lifespan and greater likelihood of achieving exceptional longevity among midlife women. Findings suggest social integration may be an important psychosocial asset to evaluate for promoting longer, healthier lives.

Keywords: relationships, health, social isolation, mortality, death

Introduction

As lifespan has increased in industrialized countries, exceptional longevity – typically defined as survival to 85 years (Newman & Murabito, 2013; Revelas et al., 2018) – has become increasingly common. Empirical evidence obtained across diverse organisms has consistently demonstrated that improvements in lifespan often co-occur with delayed morbidity (Longo et al., 2015), indicating that studying factors associated with increased longevity may yield new insights regarding how to promote both long and healthy lives (also known as "healthspan") (Lopez-Otin, Blasco, Partridge, Serrano, & Kroemer, 2013). Research on exceptional longevity has largely focused on identifying biomedical factors (e.g., genetic variants) that are associated with increased survival, but an emerging body of research has suggested non-genetic factors matter as well. Accordingly, research has begun to identify psychosocial assets, such as optimism and other facets of psychological well-being, as potential predictors of longer life (Kubzansky et al., 2018; Lee et al., in press; Steptoe, 2019).

Social relationships have also been identified as a key predictor of human health (Berkman & Krishna, 2014; Holt-Lunstad, Robles, & Sbarra, 2017). Research has demonstrated beneficial effects of social support and networks on a wide range of health outcomes (Berkman & Krishna, 2014; Holt-Lunstad et al., 2017; Trudel-Fitzgerald, Chen, Singh, Okereke, & Kubzansky, 2016), with cognitive, emotional, behavioral, and direct biological pathways proposed to explain observed associations (Berkman, Glass, Brissette, & Seeman, 2000; Cohen, 1988; Kroenke, 2018). The relationship between social relationships and premature mortality has been assessed extensively, with many studies demonstrating an association between social isolation and increased risk of premature death (Berkman & Krishna, 2014; Holt-Lunstad et al., 2017). This work has generally followed a traditional adverse-outcomes-oriented and risk-

focused perspective. However, investigators have called for applying a positive health framework to gain greater insight into how to promote and preserve healthy functioning (Lloyd-Jones, 2014; National Research Council Committee on Future Directions for Behavioral and Social Sciences Research at the National Institute of Health, 2001). This shift in priorities grows out of an increasing understanding that insights derived from considering risk factors associated with increased disease and mortality may differ from those derived from examining positive factors that may be associated with the attainment and maintenance of good health. Moreover, the absence of a harmful risk factor is not necessarily the opposite of the presence of a positive or protective factor. For example, not being socially isolated is different from being social integrated. Depending on the measure used to assess social isolation, it may not be possible to determine if an individual who does not meet criteria for social isolation is in fact truly socially integrated, without additional information. Recent studies investigating the potential role of positive factors with future risk of chronic diseases and premature mortality have found meaningful associations independent of not only conventional risk factors (e.g., health status), but also psychosocial risk factors (e.g., depressive symptoms), reinforcing the idea that positive factors capture more than merely the absence of negative factors (VanderWeele et al., in press). Yet, to our knowledge no studies have explicitly examined the association of social relationships with exceptional longevity.

Research suggests being social integrated (and other psychosocial assets) is associated with health outcomes above and beyond the effects of other risk factors (Berkman & Krishna, 2014; Holt-Lunstad et al., 2017; Steptoe, 2019). From a positive health framework, social relationships are considered as a health asset or a life skill (Steptoe & Wardle, 2017), not only reducing likelihood of specific diseases, but also leading to positive health outcomes, such as

achieving or maintaining health or healthy aging, more likely. Identifying diverse assets that promote health across the life course, particularly health in aging, will help inform efforts not only to reduce exposure to health risks, but also to achieve optimal functioning, informing a "primordial prevention" approach (Strasser, 1978). Although healthy aging is a multidimensional construct that is often defined to incorporate physical, cognitive, and emotional well-being, the achievement of long lifespan is its most basic prerequisite (Anton et al., 2015; Woods et al., 2016). By understanding assets that promote longevity, we can take a step outside the paradigm of disease and death, and create new insights regarding the means through which long and healthy lives can be achieved.

In the present study, we assessed social integration, which refers to the number, type, and frequency of social contacts, and evaluated its association with increased longevity. We focus on social integration because it has been associated with health outcomes more consistently than other social relationship constructs like emotional social support (Cohen & Janicki-Deverts, 2009; Holt-Lunstad et al., 2017; Nausheen, Gidron, Peveler, & Moss-Morris, 2009). We used data from the Nurses' Health Study, a large ongoing cohort of women, to evaluate if higher levels of social integration are associated with longer lifespan, as well as with greater likelihood of attaining exceptional longevity. All analyses controlled for potential confounders, including demographics and initial health status, following prior research in this domain.

We also considered the role of depression, because prior research has suggested that greater social integration is associated with less depression (Chang, Pan, Kawachi, & Okereke, 2016) and also that depression is related to a greater risk of premature mortality (J. Wei et al., 2019). The direction of causality between social integration and depression is uncertain (Berkman et al., 2000), but due to data limitations, we considered depression as a potential

confounder in sensitivity analyses. Since lifestyle factors are posited to lie on the pathway linking social integration to longevity, we included a separate set of models adjusting for health-related behaviors to examine explicitly whether adding these variables may partly or fully explain the associations of interest. Lastly, in secondary analyses we investigated individual domains of social integration (e.g., religious participation; number of close friends/relatives) to ascertain whether some components were differentially salient for longevity. We hypothesized that greater levels of social integration were associated with longer lifespan, as well as with greater likelihood of attaining exceptional longevity, beyond statistical adjustment for potential confounders and pathways.

Methods

Study Population

Data are from the ongoing Nurses' Health Study (NHS) cohort, which began in 1976 with 121,700 married female registered nurses aged 30 to 55 year-old. Since 1976, NHS participants have returned biennial questionnaires collecting data on health, nutrition, and lifestyle, as well as a variety of social and psychological factors, with follow-up rate ~85-90% (Bao et al., 2016). The sample for our primary analysis included women who completed the 1992 measure of social integration –the Berkman-Syme Social Network Index– and have been followed through 2014. Participants were excluded from analyses if they were missing data on social integration or demographic covariates (excluding husband's education for which we created a missing indicator because 15.51% of data was missing) or if they died within 2 years after baseline, to reduce likelihood of reverse causation whereby imminent death would influence social relationships or the reporting of them. These exclusions reduced the sample size

from 103,601 to 72,322 women. This sample size is either comparable to or larger than most prior studies investigating either social integration with various health-related outcomes (Pinquart & Duberstein, 2010; Trudel-Fitzgerald et al., 2016) or psychosocial factors with longevity (Costa, Weiss, Duberstein, Friedman, & Siegler, 2014; Lee et al., in press). Further assessment of the statistical stability of the results for this study was quantitatively evaluated by considering the width of confidence intervals (CI). For analyses assessing the likelihood of survival to the age of 85, the sample was further restricted to participants born before 1928, for whom it was possible to reach the age of 85 during the study period (N=16,818). The study protocol was approved by the institutional review boards of the Brigham and Women's Hospital.

Measures

Social integration. Social integration, a construct that captures the number, type, and frequency of social contacts, was assessed with the Berkman-Syme Social Network Index (SNI) (Berkman & Krishna, 2014; Berkman & Syme, 1979), administered via self-reported scale in 1992. The SNI assesses quantity and type of social relationships across four domains: marriage, contacts with close friends and relatives, participation in religious activities, and participation in group associations (Berkman & Syme, 1979). The measure has shown good test-retest reliability and acceptable construct validity, and has predicted breast cancer survival and mental functioning in NHS women (Trudel-Fitzgerald et al., 2016). Following prior work using the SNI in this cohort (Chang et al., 2017; Kroenke, Kubzansky, Schernhammer, Holmes, & Kawachi, 2006; Trudel-Fitzgerald et al., 2016), each of the four domains of social integration was scored from 0 (least integrated) to 3 (most integrated) (Online Resource 1). These domain scores were summed to create a continuous SNI score ranging from 0 (highly socially isolated) to 12 (highly socially integrated). The continuous SNI score was considered missing if scores for any of the

four domains were unavailable. This score was then divided into quartiles to allow for examination of potential discontinuous or threshold effects. Thus, participants were classified according to four levels of social integration: highly socially isolated (reference group), moderately isolated, moderately integrated, and highly socially integrated (Chang et al., 2017; Kroenke et al., 2006; Trudel-Fitzgerald et al., 2016). In the Nurses' Health Study, the SNI was administered every four years, covering a 16-year period from 1992 to 2008. Scores are fairly stable across assessments, as supported by a high intra-class correlation coefficient (ICC) value (ICC: 0.76, 95% CI: 0.76-0.77) and low within-subject variability (0.18, 95% CI: 0.18-0.18) in the current analytic sample. Therefore, we did not conduct additional analyses updating the SNI score or considering trajectories of change in SNI over time. Of note, to enter the cohort study when it was first initiated in 1976, women had to be married; consequently, most participants were still married or in a domestic partnership in 1992 when the SNI was first queried.

Lifespan. Lifespan was operationalized as changes in predicted lifespan. We also considered exceptional longevity, which was defined as survival to the age of 85 years or older. Deaths are reported by participants' families and by postal authorities. The names of non-respondents are searched within the National Death Index, which has compiled data from state death registries since 1979 and correctly identifies 98% of known deaths among a sample of NHS participants for whom death certificates were available (Rich-Edwards, Corsano, & Stampfer, 1994). Date of death is ascertained from death records. In the current study, deaths were identified through the end of 2014, the most recently available data.

Covariates. All covariates were queried at baseline (in 1992), unless otherwise noted. Demographic variables including age (continuous), education level (registered nurse vs. undergraduate/graduate degree), and husband's education level (≤ high school, above high

school, missing level) were considered as potential confounders. Analyses also considered self-reported prevalence or history of the following major chronic diseases, individually (yes vs. no): high cholesterol, high blood pressure, diabetes, cancer, stroke, and myocardial infarction (MI). Depressive symptoms were assessed via the five-item Mental Health Inventory (MHI-5), a subscale of the 36-Item Short Form Survey from the RAND Medical Outcomes Study (Ware & Sherbourne, 1992). Scores ranged from 0 (most depressed) to 100 (least depressed), and participants were classified as having clinical depressive symptoms (yes vs. no) if their score was ≤60 (Rumpf, Meyer, Hapke, & John, 2001).

Health behavior-related variables, such as smoking status, physical activity, alcohol consumption, diet quality, and body mass index (BMI) were considered as covariates that might either confound or potentially mediate the association between social integration and longevity. Self-reported smoking status was defined as never, former, or current smoker. Physical activity was modeled as a dichotomous variable indicating whether the participant met recommended levels of physical activity (i.e., reporting ≥150 minutes of moderate-to-vigorous physical activity per week; yes vs. no). Alcohol consumption and diet quality were assessed via a food frequency questionnaire (Yuan et al., 2017) administered in 1994. Alcohol was modeled as a dichotomous variable indicating whether participants met recommendations for no more than one serving of an alcoholic drink per day (yes vs. no) (US Department of Health and Human Services & US Department of Agriculture, 2010). Diet quality was operationalized as a continuous variable using the Alternative Health Eating Index (AHEI), which assigns a dietary score ranging from 0 (lowest quality) to 100 (highest quality) based on higher intake of vegetables, fruit, whole grains, nuts and legumes, long-chain (n-3) fatty acids, polyunsaturated fats; lower intake of sugar-sweetened beverages and fruit juice, red/processed meat, saturated fats, sodium (McCullough et

al., 2002). Body mass index (BMI) was calculated using participants' self-reported height and weight (kg/m^2). Self-reported weight has been shown to be highly correlated (r = .97) with weight measured by study staff within this cohort (Rimm et al., 1990).

Statistical Analysis

Statistical analyses were conducted using SAS, 9.4. We first computed the descriptive statistics for each covariate across levels of social integration, adjusting for age. A set of four accelerated failure time (AFT) models were used in primary analyses to estimate the proportion by which participants' lifespans differed in association with level of social integration (N=72,322). Compared to the Cox proportional hazards models, the AFT models provide the advantage of easily interpretable results (i.e., percent change in lifespan), while still incorporating longitudinal data and controlling for multiple covariates (Swindell, 2009; L. J. Wei, 1992). AFT models were shown to be a useful statistical framework for aging research (Swindell, 2009), and have been leveraged in prior studies investigating the relationship of personality (Costa et al., 2014), optimism (Lee et al., in press), and inflammation markers (Wassel, Barrett-Connor, & Laughlin, 2010), respectively, with longevity.

In the current study, a "basic" adjusted model included potential demographic confounders (i.e., age, husband's education, and participant's education). A second model, the core model, further adjusted for baseline health status variables (i.e., prevalent or history of high cholesterol, high blood pressure, MI, stroke, diabetes, and cancer). A third model included both demographic confounders and health behavior-related factors (i.e., smoking status, physical activity, alcohol consumption, diet quality, and BMI) to assess whether behaviors accounted for any of the observed association between social integration and longevity. A fourth model adjusted for all covariates simultaneously. Sample size for the third and fourth models was

slightly reduced as they were evaluated among women who had data on all health-behavior related variables (n=66,684; 92.20% of the main analytic sample). We applied the transformation $100(e^{\beta} - 1)$ to the regression coefficient for our primary exposure, social integration, to interpret the findings as the percent change in the expected survival time comparing each social integration level to the reference (highly socially isolated). A positive coefficient suggests that greater levels of social integration are associated with greater longevity.

We conducted three additional analyses. A first sensitivity analysis considered the role of depression in a subset of women who had data on depression (n=72,123; 99.72% of the main analytic sample) by evaluating changes in the effect estimates for social integration when including depressive symptoms in the core model controlling for demographic and health status covariates. A second sensitivity analysis evaluated the main models without excluding women who died within 2 years of baseline (n=72,776). Lastly, in secondary analyses, we examined whether any of the four domains of social integration (i.e., marriage, close friends/relatives, group associations and religious activities) were differentially predictive of longevity. In this analysis, we evaluated separate models, considering each domain as an independent predictor in the core AFT model described above.

We also conducted analyses using logistic regression models to assess the likelihood of survival to the age of 85 years or older, representing exceptional longevity, using the same modeling strategy described for AFT analyses (N=16,818 for Models 1 and 2; n=15,598 for Models 3 and 4 [92.75% of the main analytic sample]). No standard definition for exceptional longevity has been established; however, the cutpoint of 85 years is commonly used (Newman & Murabito, 2013; Revelas et al., 2018) because it is well beyond the average life expectancy of individuals born in the early 20th century, without being extremely rare. Secondary analyses with

the logistic regression models explored the roles of individual domains of social integration while sensitivity analyses assessed depressive symptoms (n=16,757; 99.64% of the main analytic sample) as a potential confounder and the main models without excluding deaths 2 years after study onset (n=17,016; as described above).

Results

Table 1 shows the age-adjusted distributions of covariates in 1992 by level of social integration for the primary analytic sample (i.e., the sample for AFT analyses). Over an average of 18.73 (SD=4.15) years of follow-up, about a third of this sample (n=25,723) died within the study period. Participants classified as "highly socially integrated" (highest level of social integration) had continuous SNI scores that ranged from 10-12, and the mean SNI score in the overall sample was 7.76. At the study baseline in 1992, 81.55% of participants were married, 46.10% reported having six or more close friends/relatives, 53.56% reported attending religious activities once a week or more, and 11.07% reported participating in group associations for six or more hours per week. The mean age was 58.80 years. Women categorized as highly socially integrated reported husbands having higher levels of education, were less likely to be depressed, and had healthier lifestyle (e.g., were less likely to be current or former smoker while more likely to be physically active).

Accelerated failure time analyses demonstrated a graded association between higher levels of social integration and longer lifespan (p-value for trend ≤ 0.0001 in all models; Table 2). In models adjusted for demographic variables and health status (core model), compared to women with the lowest levels of social integration, women who were moderately integrated and highly socially integrated had 7.06% (95% CI: 5.87-8.27) and 10.10% (95% CI: 8.80-11.42)

longer lifespan, respectively. These associations declined to 3.74% (95% CI: 2.60-4.89) and 4.88% (95% CI: 3.66-6.11) when health behaviors were further added to the model, but remained statistically significant. In a fully-adjusted model assessing SNI score as a continuous variable, each one-unit increase in social integration was modestly but significantly associated with a 0.69% (95% CI: 0.53-0.86) increase in lifespan.

In AFT models assessing the domains of social integration separately, all four domains were associated with increased longevity in core models controlling for demographic and health status variables (Online Resource 2). Participants with the highest versus lowest level of participation in group associations and religious activities had a lifespan 3.81% longer (95% CI: 2.49-5.14) and 6.39% longer (95% CI: 5.36-7.42), respectively. Moreover, having 6+ close friends versus none was related to a 7.39% (95% CI: 1.23-13.93) increase in lifespan, whereas being married/partnered was associated with a 6.09% increase in lifespan compared to being widowed/separated/divorced (95% CI: 5.05-7.13). In a sensitivity analysis assessing depressive symptoms as a potential confounder, findings were materially unchanged; for example, the effect estimate comparing the most to the least socially integrated participants declined slightly to 9.24% and remained statistically significant (95% CI: 7.94-10.55). Similarly, results were robust when including women who died within the first 2 years after study onset: in the core model, compared to women with the lowest levels of social integration, women who were moderately integrated and highly socially integrated had 8.12% (95% CI: 6.77-9.49) and 11.63% (95% CI: 10.15-13.13) longer lifespan, respectively.

Of the women included in analyses of exceptional longevity, 9,070 (53.93%) survived to the age of 85 or older. Similar to findings in AFT analyses, there was a graded association between higher levels of social integration and greater likelihood of exceptional longevity (*p*-

value for trend ≤0.001 in all models; Table 3). For example, in the core model, compared to highly socially isolated women, the likelihood of achieving exceptional longevity for participants who were moderately integrated and highly socially integrated was higher with odds ratios (ORs) of 1.28 (95% CI: 1.17-1.40) and 1.41 (95% CI: 1.28-1.54), respectively. These associations declined slightly, but remained statistically significant, when health behaviors were further included in the models. In a fully-adjusted model assessing SNI score as a continuous variable, the odds ratio for exceptional longevity was barely but significantly associated with a one-unit increase in social integration was 1.02 (95% CI: 1.01-1.04).

Component-specific analyses of the SNI demonstrated that greater participation in group associations, greater religious activities attendance, and currently being married/partnered were associated with greater likelihood of exceptional longevity, although there was no statistically significant association for number of close friends/relatives (Online Resource 3). In additional sensitivity analyses, effect estimates were materially unchanged (OR for highly socially integrated vs. highly socially isolated in core model=1.42, 95% CI: 1.30-1.56) when depressive symptoms were included in the model as a potential confounder or when women who died within the first 2 years of follow-up were not excluded (core model: $OR_{\text{moderately integrated vs. highly isolated}}$=1.29, 95% CI: 1.18-1.41; $OR_{\text{highly integrated vs. highly isolated}}$=1.43, 95% CI: 1.30-1.57).

Discussion

To our knowledge, this is the largest study to assess the association between social integration and lifespan, and the first to consider the association between social integration and the achievement of exceptional longevity. Consistent with our hypothesis, higher levels of social integration were associated with increased lifespan and greater likelihood of exceptional

longevity. This association persisted in models adjusting for chronic health conditions; while estimates were slightly attenuated when controlling for health behaviors, they remained statistically significant. Such attenuation is congruent with our hypothesis that health-related behaviors serve in part as pathways by which social relationships affect physical health, although further work is needed with more clear temporality between the measures of social integration and health-relate behaviors and to rule out the possibility of confounding. Similarly, due to data availability, we could not definitively assess whether depression preceded or was consequent to social integration levels; however, in sensitivity analyses controlling for depressive symptoms, effect estimates barely changed and remained statistically significant. Moreover, in all analyses, confidence intervals were fairly narrow around the effect estimates, indicating the estimates are stable. The magnitude of associations was also comparable to those observed in prior research targeting psychosocial determinants of longevity using analogous analyses (Costa et al., 2014; Lee et al., in press).

In analyses where SNI domains were assessed separately, religious activities attendance, participation in group associations, and being married/partnered were each associated with increased lifespan and likelihood of exceptional longevity, whereas number of close friends and relatives was less clearly related to these outcomes. This is consistent with previous research in the same cohort that demonstrated lower risk of coronary heart disease in relation to greater social integration using the composite measure, as well as all individual components of social integration except the close friend/relatives subdomain (Chang et al., 2017). However, other research using a breast cancer patient population from this cohort demonstrated that the composite measure and the number of close friends/relatives, but not other individual domains of social integration, were associated with greater likelihood of breast cancer survival (Kroenke et

al., 2006). These differences point to the potential specificity of associations between health and social relationships –what is beneficial in one set of circumstances (i.e., a healthy population) may be less effective in another (i.e., a patient population)– and lends support to the idea that associations of health to social integration may be context-dependent, rather than universal. At a minimum, findings in healthy versus patient populations may not be interchangeable.

A variety of mechanisms might explain the association between greater social integration and improved health outcomes. More favorable social relationships, captured for instance by social support and social integration, are associated with healthier levels of behavioral factors, including physical activity (Kroenke et al., 2017; Tay, Tan, Diener, & Gonzalez, 2013), successful management of chronic illnesses (Gallant, 2003; Tay et al., 2013), and smoking abstinence/cessation (Kroenke et al., 2017; Wagner, Burg, & Sirois, 2004). Positive social relationships may increase likelihood of experiencing psychological well-being (e.g., optimism, positive affect) (Kubzansky et al., 2018; Steptoe, 2019), which have been associated with future engagement in health-related behaviors (Kubzansky et al., 2018; Steptoe, 2019).

Social relationships may also improve health independently of health behaviors by enhancing positive affect and feelings of belonging and self-worth, which may have direct beneficial effects on physiology through neuroendocrine and immune pathways (Berkman et al., 2000; Cohen, 1988; Kroenke, 2018). Or they may buffer potentially toxic effects of adverse experiences and psychosocial distress (Berkman & Krishna, 2014; Kubzansky et al., 2018). In both cross-sectional and longitudinal observational studies, greater social integration and other positive characteristics of social relationships have been linked to improved biomarkers of metabolic function (e.g., cholesterol and blood pressure) (Yang et al., 2016; Yang, Li, & Ji, 2013) and to reduced systemic inflammation (Penwell & Larkin, 2010; Yang et al., 2016). It is

also possible that shared genetics (e.g., among biological relatives) impact both social integration and longevity. Furthermore, prior findings also showed that social relationships, including the size of one's social network, are positively associated with cognitive abilities and slower cognitive decline in midlife and older adults (Kelly et al., 2017). Results from the current study suggest health behaviors may mediate partly but not fully the social integration-longevity relationship. Thus, further research should evaluate whether biological processes and cognitive function might also be at play.

Several limitations of the present study should be noted. Findings in these primarily white women may not be generalizable to minorities or to men, as both social integration and mortality rates are different in different racial/ethnic groups and in different sexes; yet, the homogeneity of this cohort enhances the study's internal validity. As with all observational research, potential for unmeasured confounding remains possible. Nonetheless, our analyses controlled for a wide range of demographic and health status variables that may serve as confounders, including health behaviors and depressive symptoms. Because all women were married at cohort baseline (1976), most (but not all) participants were still married/partnered in 1992, hence reducing variability in the exposure at the current study baseline. However, heterogeneity increased over follow-up, as a higher proportion of women experienced separation/divorce or widowhood. Lastly, although the widely-studied SNI is considered a complex measure of social integration (i.e., assessing multiple dimensions), it does not capture the quality of these relationships, which also likely impact health-related outcomes (Kroenke, 2018). According to the Socioemotional Selectivity theory (Lockenhoff & Carstensen, 2004), individuals would progressively prioritize existing emotionally rewarding relationships over the expansion of their social network towards the end of life. As a result, it is possible that the association between larger social networks and longevity

captures the fact that younger individuals who are likely to live longer, and that such bias would not be fully accounted by statistical control for chronological age. However, in the current sample, the SNI score was highly stable over 16 years and comparable across age groups, reducing concerns that these women experienced substantial changes in the size of their social network over time. These limitations are offset by several strengths, including the use of a large and well-characterized cohort, as well as a follow-up over two decades that enabled the assessment of exceptional longevity (i.e., attaining 85 years). Another strength of the study is its prospective research design, which combined with the 2-year lag introduced in our statistical analyses and control for major health conditions at baseline, reduced concerns about the potential for reverse causation.

As longer lifespans become more achievable through improved disease prevention and medical technology, it is increasingly important to work towards a better understanding of psychosocial assets that can help promote longer and healthier lives. A greater appreciation of these assets may be able to inform our thinking about the resources or reserves that are necessary to help people successfully age with better health. Social integration, as demonstrated in these analyses, is one such health asset that may have a substantial association with longevity. Furthermore, although many efforts at intervention have fallen short, there is also evidence that social integration has the potential to be modifiable (Cohen & Janicki-Deverts, 2009; Holt-Lunstad et al., 2017; Kroenke, 2018). If we can develop effective ways to intervene on one's social environment, we may be able to develop low-cost and targeted interventions to help individuals achieve longer and healthier lives.

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Compliance with Ethical Standards

The authors do not have any potential conflicts of interest to report. The authors assume full responsibility for analyses and interpretation of these data. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional review boards of the institutional and/or national research committee (Brigham and Women's Hospital; IRB protocol number: 1999P011114) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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Table 1. Age-adjusted covariates by quartiles of social integration in 1992 (N=72,322)

	Highly socially isolated (n=13,481)	Moderately isolated (n=17,061)	Moderately integrated (n=22,881)	Highly socially integrated (n=18,899)
Age*	58.48 (7.12)	58.63 (7.21)	58.69 (7.10)	59.32 (7.09)
Registered nurse (RN) education level, %	69	69	72	69
Husband's education				
- Less or equal to high school degree, %	31	36	38	35
- More than high school degree, %	38	49	51	56
- Missing, %	32	17	11	9
Clinical depressive symptoms, %	23	17	15	9
High cholesterol, %	45	45	47	46
High blood pressure, %	36	35	34	32
Diabetes, %	6	6	5	5
Cardiovascular disease, %	3	3	2	2
Cancer, %	10	10	10	10
Smoking status				
- Never smoker, %	33	39	46	54
- Former smoker, %	44	44	42	39
- Current smoker, %	24	17	12	8
≥150 minutes of moderate-to-vigorous physical activity/week, %	50	55	55	62
Low-moderate alcohol consumption, %	88	89	91	92
Body mass index (BMI)	26.01 (5.70)	26.01 (5.32)	25.92 (5.13)	25.93 (5.08)
Alternative Healthy Eating Index score^	48.26 (10.28)	48.54 (9.91)	48.27 (9.83)	49.08 (9.55)

Table 1. Age-adjusted covariates by quartiles of social integration in 1992 (N=72,322)

	Highly socially isolated (n=13,481)	Moderately isolated (n=17,061)	Moderately integrated (n=22,881)	Highly socially integrated (n=18,899)

Note. Values are means (SD) or percentages and are standardized to the age distribution of the study population. Values of polytomous variables may not sum to 100% due to rounding. * Value is not age adjusted. ^ Higher score indicates healthier diet.

Table 2. Percent change in lifespan associated with social integration from 1992 to 2014 (N=72,322)

	Social Integration Score Quartiles							
	Highly socially isolated		Moderately isolated		Moderately integrated		Highly socially integrated	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Model 1: Demographics	0.00	Referent	5.52	4.28-6.78	7.87	6.65-9.10	11.04	9.71-12.38
Model 2: Demographics and health conditions	0.00	Referent	4.97	3.75-6.22	7.06	5.87-8.27	10.10	8.80-11.42
Model 3: Demographics and health behaviors*	0.00	Referent	2.70	1.53-3.87	3.74	2.60-4.89	4.88	3.66-6.11
Model 4: All variables*	0.00	Referent	2.37	1.22-3.54	3.22	2.10-4.36	4.33	3.13-5.56

Note.

Model 1: age, education, and husband's education

Model 2: age, education, husband's education, as well as prevalent/history of high cholesterol, high blood pressure, diabetes, cancer, stroke, and myocardial infarction

Model 3: age, education, husband's education, smoking status, physical activity, alcohol, body mass index, and the Alternative Health Eating Index (AHEI) diet index

Model 4: age, education, husband's education, as well as prevalent/history of high cholesterol, high blood pressure, diabetes, cancer, stroke, and myocardial infarction, smoking status, physical activity, alcohol, body mass index, and the Alternative Health Eating Index (AHEI)

* Sample size for these models was 66,684 because of missing data for health behaviors.

Table 3. Odds ratios for the association of social integration with survival past age of 85 (N=16,818)

	Social Integration Score Quartiles							
	Highly socially isolated		Moderately isolated		Moderately integrated		Highly socially integrated	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Model 1: Demographics	1.00	Referent	1.21	1.10-1.33	1.32	1.21-1.44	1.47	1.34-1.61
Model 2: Demographics and health conditions	1.00	Referent	1.19	1.08-1.31	1.28	1.17-1.40	1.41	1.28-1.54
Model 3: Demographics and health behaviors*	1.00	Referent	1.11	1.00-1.23	1.14	1.04-1.26	1.20	1.08-1.32
Model 4: All variables*	1.00	Referent	1.09	0.98-1.21	1.11	1.01-1.22	1.15	1.04-1.27

Note.

Model 1: age, education, and husband's education

Model 2: age, education, husband's education, as well as prevalent/history of high cholesterol, high blood pressure, diabetes, cancer, stroke, and myocardial infarction

Model 3: age, education, husband's education, smoking status, physical activity, alcohol, body mass index, and the Alternative Health Eating Index (AHEI) diet index

Model 4: age, education, husband's education, as well as prevalent/history of high cholesterol, high blood pressure, diabetes, cancer, stroke, and myocardial infarction, smoking status, physical activity, alcohol, body mass index, and the Alternative Health Eating Index (AHEI)

* Sample size for these models was 15,598 because of missing data for health behaviors.