Social Network, Social Support, and Risk of Incident Stroke
Atherosclerosis Risk in Communities Study

Mako Nagayoshi, PhD; Susan A. Everson-Rose, PhD; Hiroyasu Iso, MD, PhD; Thomas H. Mosley Jr, PhD; Kathryn M. Rose, PhD; Pamela L. Lutsey, PhD

Background and Purpose—Having a small social network and lack of social support have been associated with incident coronary heart disease; however, epidemiological evidence for incident stroke is limited. We assessed the longitudinal association of a small social network and lack of social support with risk of incident stroke and evaluated whether the association was partly mediated by vital exhaustion and inflammation.

Methods—The Atherosclerosis Risk in Communities study measured social network and social support in 13 686 men and women (mean, 57 years; 56% women; 24% black; 76% white) without a history of stroke. Social network was assessed by the 10-item Lubben Social Network Scale and social support by a 16-item Interpersonal Support Evaluation List-Short Form.

Results—During a median follow-up of 18.6 years, 905 incident strokes occurred. Relative to participants with a large social network, those with a small social network had a higher risk of stroke (hazard ratio [95% confidence interval], 1.44 [1.02–2.04]) after adjustment for demographics, socioeconomic variables, marital status, behavioral risk factors, and major stroke risk factors. Vital exhaustion, but not inflammation, partly mediated the association between a small social network and incident stroke. Social support was unrelated to incident stroke.

Conclusions—In this sample of US community-dwelling men and women, having a small social network was associated with excess risk of incident stroke. As with other cardiovascular conditions, having a small social network may be associated with a modestly increased risk of incident stroke. **(*Stroke*. 2014;45:2868-2873.)**

Key Words: epidemiology ■ inflammation ■ social support ■ stroke

See related article, p 2853.

Stroke is the fourth leading cause of death in the United States[1] and often results in serious long-term disability and reduced quality of life for both patients with stroke and their families. Therefore, stroke prevention is a public health priority.

The social environment is thought to have a tremendous influence on physical and psychological health and well-being.[2] Social network refers to the structure of one's relationships, in terms of both quality and quantity.[3] Social support refers to the functions or provisions given by one's social relationships, such as emotional concern, instrumental assistance, or information.[3] Although social support is downstream of social network,[4] measuring both variables is meaningful because not all social networks or ties are supportive and there is variation in the type, frequency, intensity, and extent of support provided.[4]

Previous epidemiological studies have demonstrated that having a small social network and lack of social support are associated with an increased incidence of coronary heart disease[5–8] and heart failure,[6,9] but relatively few studies have examined whether these factors are associated with incident stroke.[10–13] The mechanisms underlying these associations have not been fully elucidated but likely include both behavioral factors (eg, poor diet, smoking, alcohol use, and low physical activity)[14] and physiological components (eg, hypertension, diabetes mellitus, obesity, and inflammation),[15,16] which may be partly influenced by mental stress (eg, depression, loneliness, or vital exhaustion). Using data from the Atherosclerosis Risk in Communities (ARIC) study, we tested the hypotheses that small social network and lack of social support are associated with greater risk of incident stroke, independent of behavioral factors, and other major risk factors for stroke. We also examined whether these associations were partially mediated by vital exhaustion and a marker of systematic inflammation (ie, high-sensitivity C-reactive protein [hsCRP]).

Received April 15, 2014; final revision received June 27, 2014; accepted July 16, 2014.

From the Division of Epidemiology and Community Health (M.N., P.L.L.) and Department of Medicine (S.A.E.-R.), University of Minnesota, Minneapolis; Department of Community Medicine, Nagasaki University Graduate School of Biomedical Science, Nagasaki, Japan (M.N.); Department of Medicine, Osaka University, Suita, Japan (H.I.); Departments of Geriatrics/Gerontology and Neurology, University of Mississippi Medical Center, Jackson, MS (T.H.M.); and Department of Epidemiology, University of North Carolina at Chapel Hill (K.M.R.).

The online-only Data Supplement is available with this article at http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.114.005815/-/DC1.

Correspondence to Mako Nagayoshi, PhD, Department of Community Medicine, Nagasaki University Graduate School of Biomedical Science, 1-12-4 Sakamoto, Nagasaki 852–8523, Japan. E-mail mnagayoshi@nagasaki-u.ac.jp

Stroke **is available at http://stroke.ahajournals.org** **DOI: 10.1161/STROKEAHA.114.005815**

Methods

The ARIC study is a predominantly biracial prospective epidemiological cohort, which enrolled 15 792 adults aged 45 to 64 years at the baseline visit (1987–1989).[17] Participants were recruited through population-based sampling from 4 US communities: Washington County, MD; suburban Minneapolis, MN; Forsyth County, NC; and Jackson, MS. A total of 4 cohort re-examinations have taken place (1990–1992, 1993–1995, 1996–1998, and 2011–2013). Institutional review boards at each of the participating institutions approved the study, and all participants gave informed consent.

Study Population

Social network size and perceived social support were measured at visit 2 (1990–1992), which was attended by 14 348 participants and thus serves as baseline for the present analysis. We excluded 275 participants with prevalent stroke from the analysis at baseline, 42 participants whose race were not white or black, and 47 black participants from the Maryland and Minnesota study communities. We further excluded participants with incomplete data from relevant analyses on social network (n=298) and perceived social support (n=301), resulting in final analytic samples of 13 686 and 13 683, respectively.

Social Network and Perceived Social Support Assessment

Social network was measured using the 10-item Lubben Social Network Scale,[18] which assesses the size of the participant's active social network of family, friends, and neighbors. Each item ranged from 0 to 5. The total score is an equally weighted sum, with scores ranging from 0 to 50; the higher the score, the larger the social network. Consistent with previous work, 4 categories were created: score ≤20=small social network; 21 to 25=moderate small social network; 26 to 30=moderate large social network; and ≥31=large social network.[9,18]

Perceived social support was measured using a modified version of the Interpersonal Support Evaluation List-Short Form.[19] This 16-item scale was constructed by previous ARIC investigators from the original 40-item scale[20] and assesses perceived social support with 4 subscales (1) appraisal support, (2) tangible assets support, (3) belonging support, and (4) self-esteem support. Each item has choices as definitely false to definitely true, and the score ranges from 0 to 3. The total score is an equally weighted sum, with scores ranging from 0 to 48; the higher the score, the greater the perceived social support. There is no standard interpretation for this score. In the present analysis, we interpreted the score as follows: ≤16=lack of social support; 17 to 23=low social support; 24 to 31=moderate social support; and ≥32=high social support.

Measurement of Covariates and Potential Mediators

Information on covariates and potential mediators was assessed at ARIC visit 2, except educational attainment, which was assessed at ARIC visit 1. Questionnaires were used to attain information on age, sex, race, socioeconomic status (including educational attainment, income, and occupation), marital status, smoking status, alcohol use, and medications. Vital exhaustion was measured using the 21-item Maastricht Questionnaire to characterize excessive fatigue, irritability, and feelings of demoralization.[21] Higher scores indicate greater exhaustion.

Physiological variables were measured by trained technicians. Body mass index was assessed as weight (kg) divided by height (m) squared. Hypertension was defined as diastolic blood pressure ≥90 mm Hg, systolic blood pressure ≥140 mm Hg, or self-reported antihypertensive medication use during the previous 2 weeks. Diabetes mellitus was defined as fasting serum glucose level ≥126 mg/dL, nonfasting glucose ≥200 mg/dL, or self-reported history of physician-diagnosed diabetes mellitus or medication use for diabetes mellitus during the past 2 weeks. Cholesterol was measured enzymatically. Low-density lipoprotein was calculated. hsCRP was measured in serum using a latex-particle–enhanced immunoturbidimetric assay kit (Roche Diagnostics).

Stroke Ascertainment

Possible stroke events were identified through annual follow-up phone calls to participants or proxies, which asked about recent hospitalizations and deaths, surveillance of discharges from local hospitals, and death certificates. Medical records were obtained if the list of discharge diagnoses included an *International Classification of Diseases*, 9th Revision, code of 430 to 438, if a cerebrovascular condition or procedure was mentioned in the discharge summary, or if a cerebrovascular finding was noted on a computed tomography or magnetic resonance imaging report. Abstractors recorded stroke signs and symptoms and photocopied neuroimaging (computed tomography or magnetic resonance imaging) and other diagnostic reports.

Each potential stroke case was classified by computer algorithm and by physician reviewers according to criteria adapted from the National Survey of Stroke.[22] Disagreements were adjudicated. Qualifying strokes were classified as definite or probable ischemic stroke (neuroimaging showed acute infarction or no hemorrhage) or hemorrhagic stroke (intraparenchymal or subarachnoid) on the basis of neuroimaging studies or autopsy, when available.

Statistical Analysis

Descriptive statistics of covariates and potential mediators, according to categories of social network score and perceived social support score, were generated using ANOVA and χ^2 tests, as appropriate. Pearson correlation coefficients were calculated. Cox proportional hazards regression model were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for incident total stroke, by categories of social network and social support, after sequential adjustment for potential confounding variables. In secondary analyses, we also looked separately at ischemic and hemorrhagic stroke. Follow-up time was calculated from the date of the visit 2 examination until the date of the incident stroke, loss-to-follow-up, death, or December 31, 2010, whichever came first.

We fit 4 sequential models: model 1 adjusted for age, sex, and race; model 2 additionally adjusted for socioeconomic and marital status; model 3 further adjusted for behavioral risk factors (smoking status, alcohol use, and physical activity); and model 4 additionally adjusted for major stroke risk factors (hypertension, diabetes mellitus, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, lipid-lowering medication use, and body mass index). We further added to model 4 covariates vital exhaustion, and separately hsCRP, to assess whether they mediated the associations. Mediation was suggested if regression coefficients changed by ≥10%. In secondary analyses, we looked separately at ischemic and hemorrhagic stroke. We also examined whether either race or sex modified the relationships between social network or perceived social support and incident stroke, by including cross-product terms in the models. The proportional hazards assumption was tested by log-rank tests with Kaplan–Meier curves. All analyses were performed using SAS 9.3 (SAS Institute Inc).

Results

The 13 686 participants in our final analytic sample were on average 57 years old, 56% women, and 24% black. During a median follow-up of 18.6 years (max=20.9 years), a total of 905 incident strokes occurred (114 hemorrhagic strokes and 804 ischemic strokes), yielding a crude total stroke incidence of 4.0 per 1000 person-years.

The social network score was correlated with perceived social support (r=0.49; P<0.0001) and vital exhaustion (r=-0.21; P<0.0001) but not with hsCRP (r=–0.01; P=0.46). The perceived social support score was correlated with vital exhaustion (r=–0. 41; P<0.0001) and hsCRP (r=–0.04; P<0.0001).

Small Social Network

Table 1 shows the age-adjusted characteristics of participants according to social network size categories at

Table 1. Age-Adjusted Demographic, Behavioral, and Physiological Characteristics Stratified by Social Network Size: The Atherosclerosis Risk in Communities Study 1987 to 1989

	Small Social Network	Moderately Small Social Network	Moderately Large Social Network	Large Social Network
Social Network Score	≤20	21–25	26–30	≥31
n	380	778	1908	10620
Demographics				
Age, y*	57.1 (5.7)	57.1 (5.8)	57.2 (5.9)	56.9 (5.7)
Men, %	58.1	52.4	49.3	42.5
White, %	67.8	70.5	73.0	77.2
Married, %	42.0	53.9	65.3	84.9
Socioeconomic status				
Income, %†				
<$25 000	60.0	50.3	40.4	32.4
$25 000–$49 999	29.1	32.0	37.9	39.5
≥$50 000	10.9	17.8	21.7	28.1
Education, %†				
Less than high school	33.8	25.9	23.1	20.2
High-school graduate	37.7	38.5	41.7	42.0
Beyond high school	28.5	35.6	35.2	37.8
Occupation, %				
Employed	65.0	69.8	73.4	70.1
Managerial and professional	16.5	20.1	24.3	23.7
Social network (0–50)*	16.9 (3.5)	23.3 (1.4)	28.3 (1.4)	37.7 (4.2)
Family networks	5.8 (3.3)	7.8 (2.9)	9.3 (2.3)	12.2 (1.9)
Friends networks	2.8 (3.1)	4.9 (3.4)	6.6 (2.8)	9.6 (2.4)
Confidant relationship	3.6 (1.8)	5.0 (1.8)	5.7 (1.8)	7.2 (1.6)
Helping arrangements	2.2 (1.8)	2.7 (1.7)	3.1 (1.6)	4.2 (1.3)
Living arrangements	2.6 (2.4)	3.0 (2.3)	3.6 (2.1)	4.6 (1.2)
Social support (0–48)*	26.6 (7.5)	31.3 (6.9)	33.8 (6.6)	38.3 (5.7)
Behavioral risk factors				
Physical activity*	2.3 (0.8)	2.3 (0.8)	2.4 (0.8)	2.5 (0.8)
Current drinkers, %	55.4	59.0	57.1	56.7
Current smokers, %	35.9	29.0	27.5	20.3
Major stroke risk factors				
BMI, kg/m^2*	27.7 (5.6)	27.6 (5.3)	27.8 (5.4)	28.0 (5.4)
Hypertension, %	41.1	40.4	41.6	40.2
Diabetes mellitus, %	19.1	16.7	13.9	14.5
Lipid-lowering medication use, %	3.9	6.4	6.6	6.3
Low-density lipoprotein, mg/dL*	134.2 (35.0)	131.5 (38.2)	132.7 (35.7)	133.6 (36.9)
High-density lipoprotein, mg/dL*	49.7 (20.1)	49.2 (16.5)	49.1 (17.0)	49.7 (16.6)
Potential mediators				
Vital exhaustion* (0–42)	16.7 (11.3)	13.8 (10.5)	11.7 (9.3)	9.6 (8.1)
Highly vital exhausted (≥14), %	55.5	43.8	36.7	27.4
hsCRP, mg/dL*	5.0 (8.6)	4.6 (8.7)	4.3 (6.4)	4.3 (6.7)

BMI indicates body mass index; and hsCRP, high-sensitivity C-reactive protein.
*Represented as mean (SD).
†Not adjusted for age.

baseline. A total of 380 (2.8%) were classified as having a small social network. Relative to people with a large social network, those with a small social network were more likely to be black, male, not married, unemployed, have a high score on the vital exhaustion measure, be diabetic, smokers, have low income, low educational attainment, and higher hsCRP (Table 1). Among participants with a small social network, 9.2% were classified as lacking social support based on the Interpersonal Support Evaluation List-Short Form responses.

Table 2. Social Network Size and Risk of Incident Stroke: The Atherosclerosis Risk in Communities Study 1987 to 2010

	Social Network Score			
	Small Social Network ≤20	Moderately Small Social Network 21–25	Moderately Large Social Network 26–30	Large Social Network ≥31
No. of participants	380	778	1908	10620
Person-years	5867	12541	31002	178775
Total incident strokes	41	51	119	694
Model 1	1.60 (1.17–2.20)	0.98 (0.73–1.30)	0.93 (0.77–1.13)	1.00
Model 2	1.43 (1.03–2.00)	0.92 (0.69–1.23)	0.90 (0.73–1.10)	1.00
Model 3	1.36 (0.97–1.90)	0.89 (0.66–1.20)	0.87 (0.71–1.06)	1.00
Model 4	1.44 (1.02–2.04)	0.93 (0.69–1.26)	0.90 (0.73–1.11)	1.00

Model 1: adjust for age, sex and race; model 2: adjusted for model 1+socioeconomic status (education attainment, income, and occupation)+marital status; model 3: adjusted for model 2+behavioral risk factors (smoking status, alcohol drinking, and physical activity); and model 4: adjusted for model 3+major stroke risk factors (hypertension, diabetes mellitus, low-density lipoprotein, high-density lipoprotein, lipid-lowering medication use, and body mass index).

The relationship between social network and risk of incident stroke was nonlinear; only those in the small social network group were at greater risk (Table 2). The age, sex, and race-adjusted HR for those classified as having a small social network was 1.60 (95% CI, 1.17–2.20), relative to those with a large social network. Results were only slightly attenuated with further adjustment for socioeconomic status and marital status (model 2, 1.43 [1.03–2.00]), behavioral risk factors (model 3, 1.36 [0.97–1.90]), and major stroke risk factors (model 4, 1.44 [1.02–2.04]). There was no evidence that either race or sex modified relationships between small social network and incident stroke.

Vital exhaustion and hsCRP, possible mediators, were both associated with incident stroke in age, sex, and race-adjusted models (HR [95% CI] for 1-point higher vital exhaustion score, 1.02 [1.01–1.03]; HR for 1 mg/dL higher hsCRP, 1.02 [1.01–1.03]). The β for small social network in model 4 was 0.366. With additional adjustment for vital exhaustion, the β was 0.336 (an 8.1% change), whereas with adjustment for hsCRP it was 0.361 (a 1.4% change). These results suggest that vital exhaustion, but not hsCRP, may partially mediate the association between small social network and incident stroke.

In secondary analyses, we looked separately at small social network and risk of ischemic stroke and hemorrhagic stroke. The associations of ischemic stroke were similar to those of total stroke (eg, model 4: HR, 1.41 [0.98–2.03]), as expected because 89% of total strokes were classified as ischemic (Table I in the online-only Data Supplement). There were too few hemorrhagic strokes to examine separately.

Perceived Social Support

A total of 75 participants (0.5%) were classified as lacking perceived social support. Associations between perceived social support categories and participant characteristics (Table II in the online-only Data Supplement) were, overall, similar to those observed with stratification by social network size. Among the lack of social support group, 46.6% were also classified as having a small social network.

Only 7 cases of incident stroke occurred in the lack of social support group. Relative to those with high social support, participants in the lack of social support group were at qualitatively higher although not significantly higher, risk of incident stroke (model 1: HR, 1.66 [0.79–3.50]; Table III in the online-only Data Supplement). The estimate was attenuated with adjustment for additional confounding factors (models 2–4). Associations between degree of social support and risk of ischemic stroke were similar to those for total stroke (data not shown). In secondary analyses, we defined lack of social support more broadly, comparing those in the lowest quintile of social support (score, ≤31) with those in the highest quintile (score, ≥43). The HR (95% CI) observed for model 1 was 1.14 (0.93–1.39).

Discussion

In this population-based longitudinal study of 13686 participants, those who reported having a small social network were at ≈40% greater risk of incident stroke, relative to their counterparts who reported a large social network. This association was independent of participant demographics, behavioral factors, body mass index, and traditional stroke risk factors. Although this suggests a causal association, our results need to be interpreted cautiously given the observational nature of the data. While not statistically significant, participants in our sample reporting lack of social support tended to be at qualitatively higher risk of stroke.

Our results are consistent with a previous study of 32624 US male health professionals, which reported that men with a small social network (5.8% of their sample) experienced a 2-fold higher risk of incident stroke during 4 years of follow-up.[10] Having a small social network also has been associated with risk of incident stroke in a population of women with suspected myocardial infarction.[12] Another study of 2603 Health Maintenance Organization members randomly sampled in 1970 to 1971 and followed for 15 years reported no association between small social network and incident stroke.[11] However, this study defined a small social network by having a score in the lowest tertile of scores on a social network scale. It is possible that only individuals with a small social network are at greater risk of incident stroke, in which case the cut point

selected may not have effectively identified people who had a truly limited social network. Notably, it is difficult to make direct comparisons across these studies because different questionnaires were used to measure social network size, and different cut points employed to designate small social networks.

The mechanisms underlying the association between small social network and incident cardiovascular disease have not been fully elucidated but likely include both behavioral and physiological components. Individuals who have a small social network may be less likely to take part in health-promoting behaviors (eg, consuming a healthy diet, exercising, and not smoking),[14] and may be less likely to follow medical recommendations (eg, taking medications).[23] Additionally, psychological stress is correlated with small social network[24] and may also affect the cardiovascular system via various mental and physical changes.[15] Activation of the hypothalamic–pituitary adrenal axis is an adaptive response to stress, however prolonged stress or hypothalamic–pituitary adrenal activation is deleterious because sustained elevations in glucocorticoids may compromise the neuroimmune system or neuronal survival after an ischemic attack.[15] Previous epidemiological studies have reported that people who have a small social network score are more likely to have elevated circulating levels of hsCRP and interleukin-6.[16]

In our analysis, vital exhaustion partly mediated the relationship between small social network and risk of incident stroke. Although vital exhaustion overlaps more strongly with somatic depressive symptoms (eg, fatigue, sleep disturbance, or appetite change) than cognitive-affective depressive symptom (eg, guilt, feelings of worthlessness, and suicidal thoughts), they are highly correlated.[25] Depression, which is linked to elevated inflammatory marker levels,[26] has been associated with stroke morbidity, mortality,[27] and incidence[28] in meta-analyses and systematic reviews.

In the ARIC cohort, lack of perceived social support was not significantly associated with risk of incident stroke. Importantly, this analysis was underpowered because a small proportion of our study sample was in the lowest social support category (ie, 0.5%, who went on to experience 7 incident strokes). The optimum cutoff point for the social support scale used in ARIC is unknown.

Our study findings should be interpreted in light of several limitations. Although social network was assessed using a validated questionnaire, the abbreviated 16-item social support scale was constructed by earlier ARIC investigators from the original 40-item full scale[20] and was not validated. Measurement error (and subsequent misclassification) in both social network and social support certainly occurred because the data were self-reported, and these questionnaires were administered at a single point in time (in some instances many years before the incident stroke event). Although we do not know how each individual's social network changed across time, as adults age the size of their social network typically becomes progressively smaller.[29] Second, because the prevalences of small social network and of lack of social support were low (only 2.8% and 0.5%, respectively), we had limited power to detect associations with stroke events. Third, although we adjusted for potential confounders, residual confounding or unmeasured confounders (such as depression or health services use) may have influenced the relationship between small social network and incident stroke through other pathways. Despite these limitations, our study has several strengths. The ARIC study has a wealth of information on potential confounding factors, which allowed us to examine whether the relationship between small social network and incident stroke was independent of many known risk factors. Also, stroke events in the ARIC study were adjudicated, using a standardized protocol.

In summary, having a small social network was independently associated with increased risk of incident stroke in a community-dwelling sample of black and white men and women. Vital exhaustion partly mediated this association, whereas hsCRP did not. This study adds to the literature documenting the effect of social factors and relationships on health outcomes. If the observed association was found to be causal, it would argue for encouraging health professionals to screen for network size and discuss the importance of social connections for the health and well-being with their patients, and when appropriate, providing information about community resources that offer opportunities for enhancing one's social network.

Acknowledgments

We thank the staff and participants of the Atherosclerosis Risk in Communities study for their important contributions.

Sources of Funding

The Atherosclerosis Risk in Communities study is performed as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C, HHSN268201100006C, HHSN268201100007C, HHSN268201100008C, HHSN268201100009C, HHSN268201100010C, HHSN268201100011C, and HHSN268201100012C).

Disclosures

None.

References

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation*. 2014;129:e28–e292.
2. Everson-Rose SA, Lewis TT. Psychosocial factors and cardiovascular diseases. *Annu Rev Public Health*. 2005;26:469–500.
3. Arthur HM. Depression, isolation, social support, and cardiovascular disease in older adults. *J Cardiovasc Nurs*. 2006;21(5 suppl 1):S2–S7, quiz S8.
4. Berkman LF, Glass T, Brissette I, Seeman TE. From social integration to health: Durkheim in the new millennium. *Soc Sci Med*. 2000;51:843–857.
5. Hemingway H, Marmot M. Evidence based cardiology: psychosocial factors in the aetiology and prognosis of coronary heart disease. Systematic review of prospective cohort studies. *BMJ*. 1999;318:1460–1467.
6. Eng PM, Rimm EB, Fitzmaurice G, Kawachi I. 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;155:700–709.
7. Rosengren A, Wilhelmsen L, Orth-Gomér K. Coronary disease in relation to social support and social class in Swedish men. A 15 year follow-up in the study of men born in 1933. *Eur Heart J*. 2004;25:56–63.
8. André-Petersson L, Hedblad B, Janzon L, Ostergren PO. Social support and behavior in a stressful situation in relation to myocardial infarction and mortality: who is at risk? Results from prospective cohort study "Men born in 1914," Malmö, Sweden. *Int J Behav Med*. 2006;13:340–347.
9. Cené CW, Loehr L, Lin FC, Hammond WP, Foraker RE, Rose K, et al. Social isolation, vital exhaustion, and incident heart failure: findings from the Atherosclerosis Risk in Communities Study. *Eur J Heart Fail*. 2012;14:748–753.

10. Kawachi I, Colditz GA, Ascherio A, Rimm EB, Giovannucci E, Stampfer MJ, 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;50:245–251.
11. Vogt TM, Mullooly JP, Ernst D, Pope CR, Hollis JF. Social networks as predictors of ischemic heart disease, cancer, stroke and hypertension: incidence, survival and mortality. *J Clin Epidemiol*. 1992;45:659–666.
12. Rutledge T, Linke SE, Olson MB, Francis J, Johnson BD, Bittner V, et al. Social networks and incident stroke among women with suspected myocardial ischemia. *Psychosom Med*. 2008;70:282–287.
13. Ikeda A, Iso H, Kawachi I, Yamagishi K, Inoue M, Tsugane S; JPHC Study Group. Social support and stroke and coronary heart disease: the JPHC study cohorts II. *Stroke*. 2008;39:768–775.
14. Knox SS, Uvnäs-Moberg K. Social isolation and cardiovascular disease: an atherosclerotic pathway? *Psychoneuroendocrinology*. 1998;23:877–890.
15. Stuller KA, Jarrett B, DeVries AC. Stress and social isolation increase vulnerability to stroke. *Exp Neurol*. 2012;233:33–39.
16. Loucks EB, Sullivan LM, D'Agostino RB Sr, Larson MG, Berkman LF, Benjamin EJ. Social networks and inflammatory markers in the Framingham Heart Study. *J Biosoc Sci*. 2006;38:835–842.
17. The ARIC Investigators. The Atherosclerosis Risk in Communities (ARIC) study: design and objectives. *Am J Epidemiol*. 1989;129:687–702.
18. Lubben JE. Assessing social networks among elderly populations. *Fam. Community Health*. 1988;11:42–52.
19. Payne TJ, Andrew M, Butler KR, Wyatt SB, Dubbert PM, Mosley TH. Psychometric Evaluation of the Interpersonal Support Evaluation List-Short Form in the ARIC Study Cohort. *SAGE Open*. 2012;2:1–8.
20. Cohen S, Hoberman HM. Positive events and social supports as buffers of life change stress. *J Appl Soc Psychol*. 1983;13:99–125.
21. Appels A, Mulder P. Excess fatigue as a precursor of myocardial infarction. *Eur Heart J*. 1988;9:758–764.
22. Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, et al. Stroke incidence and survival among middle-aged adults: 9-year follow-up of the Atherosclerosis Risk in Communities (ARIC) cohort. *Stroke*. 1999;30:736–743.
23. Untas A, Thumma J, Rascle N, Rayner H, Mapes D, Lopes AA, et al. The associations of social support and other psychosocial factors with mortality and quality of life in the dialysis outcomes and practice patterns study. *Clin J Am Soc Nephrol*. 2011;6:142–152.
24. DeVries AC, Craft TK, Glasper ER, Neigh GN, Alexander JK. 2006 Curt P. Richter award winner: social influences on stress responses and health. *Psychoneuroendocrinology*. 2007;32:587–603.
25. Kopp MS, Falger PR, Appels A, Szedmák S. Depressive symptomatology and vital exhaustion are differentially related to behavioral risk factors for coronary artery disease. *Psychosom Med*. 1998;60:752–758.
26. Hurley LL, Tizabi Y. Neuroinflammation, neurodegeneration, and depression. *Neurotox Res*. 2013;23:131–144.
27. Pan A, Sun Q, Okereke OI, Rexrode KM, Hu FB. Depression and risk of stroke morbidity and mortality: a meta-analysis and systematic review. *JAMA*. 2011;306:1241–1249.
28. Dong JY, Zhang YH, Tong J, Qin LQ. Depression and risk of stroke: a meta-analysis of prospective studies. *Stroke*. 2012;43:32–37.
29. Wrzus C, Hänel M, Wagner J, Neyer FJ. Social network changes and life events across the life span: a meta-analysis. *Psychol Bull*. 2013;139:53–80.