


# Social relationship quality, depression and inflammation: A cross-cultural longitudinal study in the United States and Tokyo, Japan

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## Abstract

**Background:** Depression is an illness with biological, psychological, and social underpinnings, which may include the interplay of inflammation, psychological traits, stress, social relationships, and cultural background.

**Aims:** This work examines the prospective associations between social relationship quality and depressive symptoms, and between social relationship quality and inflammatory outcomes in two distinct cultures.

**Methods:** Data were obtained from two longitudinal, prospective cohort studies: Midlife in the United States (MIDUS), and Midlife Development in Japan (MIDJA) between 2004 and 2010. One thousand three hundred and twenty-seven community-based adults were included in analyses, 1,054 from the United States and 273 from Tokyo, Japan. Depressive symptoms (measured by the CES-D Depression Scale) and inflammation (measured by blood sample concentrations of the inflammatory biomarkers interleukin-6 and C-reactive protein) were the outcomes. Social relationship quality was the predictor. Culture, trait independence and interdependence, and psychosocial stressors were examined as moderators of the link between social relationship quality and depressive symptoms.

**Results:** Higher social relationship quality was associated with lower depressive symptoms in the United States ( $\beta = -6.15, p < .001$ ), but not in Japan ( $\beta = -1.25, p = .390$ ). Social relationship quality had no association with inflammation. Psychosocial stressors moderated the link between social relationship quality and depressive symptoms in both the United States ( $\beta = -0.39, p = .001$ ) and Tokyo ( $\beta = -0.55, p = .001$ ), such that social relationship quality acted as a buffer against depressive symptoms as psychosocial stress increased.

**Conclusion:** Improving the perceived quality of social relationships appears to be a stronger target for depression interventions in the United States than in Tokyo, Japan.

## Keywords

Cultural differences, social relationships, depression, health psychology, psychoneuroimmunology

## Introduction

Humans have evolved with a deep and underlying need for social ties with other humans. In modern life, the development and maintenance of social relationships with family, friends, and others continue to play a vital role in well-being. Decades of research across a wide range of demographic groups and countries have documented myriad negative health sequelae, including depression and immune dysfunction, of deficiencies in social relationships (Barger et al., 2014; Cohen & Wills, 1985; Holt-Lunstad et al., 2010; Schuster et al., 1990; Shor et al., 2013; Teo et al., 2013; Walen & Lachman, 2000; Yang et al., 2014). Interventions aiming to increase social support – one of the key components of social relationships (Vanderhorst & McLaren, 2005) – have had reasonable

success in protecting against the development of depression (Hogan et al., 2002). Nonetheless, comparisons of social relationships across countries are rare (Glei et al.,

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2012; Lansford et al., 2005), and understanding of how culture might moderate associations between social relationships and depression is lacking (Santini et al., 2015).

Research on the links between social relationships and health outcomes has shown that it is essential to consider both the supportive and straining aspects of relationships (Gilman et al., 2013; Teo et al., 2013; Walen & Lachman, 2000; Yang et al., 2014). Further, objective measures of social relationship quality, such as the frequency of social interaction, seem to be less clearly related to mental health than subjective components, such as how positive one feels about one's relationships (Barger et al., 2014; Cacioppo et al., 2010; McDade et al., 2006). Research has been unclear on how different kinds of relationships (e.g. spouse, friend, family, parental) relate to well-being, the roles of moderating factors such as gender and age on this connection (Teo et al., 2013; Walen & Lachman, 2000), and the extent to which social relationship quality and well-being are bidirectionally related (Barger et al., 2014). Psychosocial stressors related to interpersonal conflict are strongly linked to depression (Cohen & Wills, 1985; Hammen, 2005), so they may be a viable moderator by which social relationships relate to depressive symptoms. There is an ongoing debate as to whether social support directly affects depression outcomes, or instead "buffers" the effects of psychosocial stressors on depressive symptoms when stressors are high and it is needed most (Aneshensel & Stone, 1982; Cohen & Wills, 1985; Park et al., 2013).

One of the proposed biological mechanisms for some of the deleterious health effects of deficiencies in social relationships is chronic low-grade inflammation (Kiecolt-Glaser et al., 2010; Miller & Raison, 2016). There is considerable observational research suggesting that levels of inflammatory biomarkers such as C-reactive protein (CRP) and interleukin-6 (IL-6) are associated with depression (Felger et al., 2016; Furtado & Katzman, 2015; Kiecolt-Glaser et al., 2010; Loftis et al., 2013), as well as with aspects of social relationship quality (Kiecolt-Glaser et al., 2010; Yang et al., 2014, 2016). Although other pro-inflammatory cytokines (e.g. IL-1beta, TNF-alpha) are associated with depressive symptoms (Anisman et al., 1999; Loftis et al., 2008), the inflammatory factors IL-6 and CRP repeatedly emerge as depressive biomarkers in meta-analyses (Howren et al., 2009; Valkanova et al., 2013). These findings have been strengthened by studies showing that eliciting psychosocial stress causes an acute increase in inflammatory signaling via nuclear factor kappa B (Bierhaus et al., 2003), an inducible transcription factor that promotes the expression of several pro-inflammatory cytokines, including IL-6 (Liu et al., 2017), which in turn stimulates CRP production (Del Giudice & Gangestad, 2018). Further, inflammation modulates individuals' cognitive perceptions of social processes by boosting threat-related neural sensitivity to negative social experiences and increasing reward-related neural sensitivity to positive social experiences (Eisenberger et al., 2017; Iob et al.,

2019). Thus, social relationship quality, depressive symptoms, and chronic low-level inflammation may all be co-regulating phenomena (Eisenberger et al., 2017). However, the scientific literature is mixed, as other studies have not found support for these associations (Cassano et al., 2017; de Menezes et al., 2017).

On a cultural level, psychological research has identified many potential differences between countries in the East and West (Markus & Kitayama, 1991). One of the recurring themes of this literature has been that Western countries (such as the United States) are more individualistic and independent, while East Asian countries (such as Japan) are more holistic and interdependent (Markus & Kitayama, 1991). Individuals high in trait independence view themselves as distinct and wholly separate from others around them, while those high in trait interdependence feel inextricably connected to close others (Markus & Kitayama, 1991). Researchers have argued that in Japan, perceived emotional support highlights culturally endorsed values of interdependence, while in the United States perceived emotional support compromises one's ever-important sense of independence (Park et al., 2013; Uchida et al., 2008). Yet, some work has questioned the empirical basis for such claims (Diener & Diener, 1995; Matsumoto, 1999; Oyserman et al., 2002).

If the nature and subjective experience of social relationships indeed differ across cultural contexts, it follows that social relationships' impacts on health may differ cross-culturally as well. Supporting this reasoning, one study showed that the acute effects on psychological and biological outcomes of requesting social support differed based on individuals' cultural backgrounds (Taylor et al., 2007). Further, some cross-cultural studies have found that among Japanese, but not Americans, higher perceived social support is associated with fewer chronic health problems (Park et al., 2013) and greater well-being (Uchida et al., 2008).

Taken together, these data suggest that social relationships are predictive of psychological and biological outcomes, but important questions remain about the mechanisms driving and moderating this connection. Drawing from harmonized datasets from the United States and Tokyo, Japan, the present study attempts to develop a more complete picture of prospective connections between culture, social relationships, and depression. While most previous work in this area has been cross-sectional, the time gap between the collection of predictor and outcome variables in this study helps to rule out potential confounds, such as life events with impacts on both social relationships and depressive symptoms. This paper's primary hypothesis is that culture moderates the links between social relationship quality and depression and between social relationship quality and inflammation. Its secondary hypothesis is that trait independence, trait interdependence, and psychosocial stressors each moderate the link between social relationship quality and depression.

## Material and methods

### Sample

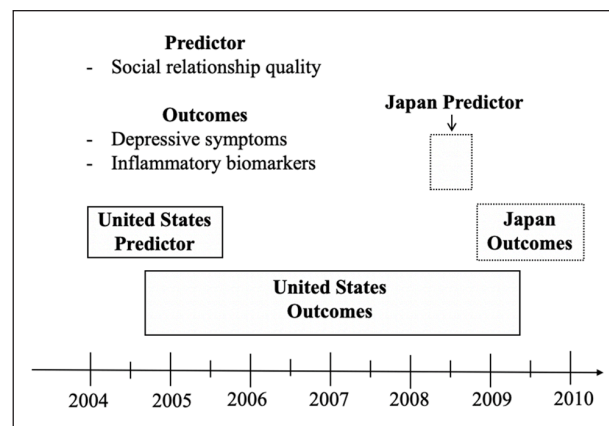
Participants from the United States were drawn from the Midlife in the United States (MIDUS) study, a national prospective cohort study of non-institutionalized English speakers. In the current study, individuals who participated in the MIDUS II biomarker project, which was conducted from 2004–2009, were examined. These individuals had also participated in the MIDUS II survey study (2004–2006). Detailed study recruitment and other procedures for MIDUS have been described elsewhere (Radler, 2014).

Japanese participants were from the National Survey of Midlife Development in Japan (MIDJA), a prospective cohort study of adults in Tokyo, Japan. In the present study, individuals who participated in the MIDJA I biomarker project, which ran from 2009–2010 were examined. As with the United States sample, these individuals had participated in the 2008 MIDJA I survey study. All Japanese participants examined in this study had at least one family member who did not live with them at MIDJA I. Detailed study procedures have been previously described (Radler, 2014).

Harmonization of measures between MIDUS and MIDJA allows for cross-cultural comparisons. All data in the present study come from United States participants who completed MIDUS II and MIDUS II Biomarker ( $n=1,054$ ), and Tokyo participants who completed MIDJA I and MIDJA I Biomarker ( $n=273$ ). Predictors were evaluated at the MIDJA I and MIDUS II timepoints, while outcomes were evaluated at the MIDJA I Biomarker and MIDUS II Biomarker timepoints. The time lag between predictor and outcome data collection was 0–5 years in the United States (mean 2.3 years) and 1–2 years in Tokyo. Moderators were evaluated at the MIDJA I baseline timepoint in the Tokyo sample and the MIDUS II Biomarker timepoint in the United States sample. Data collection timepoints are illustrated in Figure 1. Detailed information on survey methods and data collection are available online at <http://www.icpsr.umich.edu/icpsrweb/NACDA/series/00203> and in print (Radler, 2014).

### Measures

**Depressive symptoms (outcome).** Depressive symptoms were measured using the Center for Epidemiological Studies Depression scale (CES-D), a 20-item depression measure, with a higher score indicating higher depressive symptomatology (MIDUS Cronbach's  $\alpha=0.89$ , MIDJA Cronbach's  $\alpha=0.80$ ) (Radloff, 1977). The CES-D has good reliability and validity across diverse populations (Radloff, 1977) and was effective in detecting major depressive disorder in Japan (Wada et al., 2007). It has sensitivity of 0.87 (95% CI: 0.82–0.92), specificity of 0.70 (95% CI: 0.65–0.75), and diagnostic odds ratio of 16.2 (95% CI: 10.49–25.10), although it is not recommended as a diagnostic measure of depression (Vilagut et al., 2016).



**Figure 1.** Data collection time periods. The analytic sample from Japan consisted of 273 subjects who participated in both the MIDJA I Survey and MIDJA I Biomarker. The analytic sample from the United States consisted of 1,054 subjects who participated in the MIDUS 2 Survey and MIDUS 2 Biomarker.

**Inflammation (outcome).** The biomarkers IL-6 and CRP were obtained from blood samples and used to assess inflammation. Samples were processed using standardized procedures and sent to the MIDUS Biocore Lab for analysis. IL-6 concentrations were measured using blood serum and enzyme-linked immunosorbent assay (ELISA), with a reference range of 0.45–9.96 pg/mL. CRP concentrations were measured using blood plasma and immunonephelometry, with a sensitivity of  $\leq 3 \mu\text{g/mL}$ . In the United States sample, blood samples were drawn in the morning after a 12-hour fast; and in the Tokyo sample, blood samples were drawn at any point during the day, and participants were encouraged to fast for an hour before their blood was drawn. Biomarker values were not log-transformed and no cases were excluded from analyses.

**Social relationship quality (predictor).** Social relationship quality data came from self-administered survey responses assessing both social support and social strain (Radler, 2014). To evaluate social support, specifically *perceived availability of emotional support*, eight survey items were used about friends and family (Schuster et al., 1990; Walen & Lachman, 2000). Sample items included “How much do your friends really care about you” and “How much do your family members understand the way you feel about things.” Response choices ranged from 1 (“Not at all”) to 4 (“A lot”). Items demonstrated adequate internal reliability (MIDUS  $\alpha=0.86$ , MIDJA  $\alpha=0.84$ ). To evaluate *social strain*, eight survey items were used such as “How often do your family members make too many demands on you?” and “How often do your friends criticize you” (Schuster et al., 1990; Walen & Lachman, 2000). Response choices ranged from 1 (“Not at all”) to 4 (“A lot”). Items demonstrated adequate internal reliability (MIDUS  $\alpha=0.86$ , MIDJA  $\alpha=0.84$ ). *Social relationship quality* was

assessed as a composite, or average, of social support and reverse-scored social strain for friends and family. These items also demonstrated adequate internal reliability (MIDUS  $\alpha=0.80$  MIDJA  $\alpha=0.71$ ).

**Culture (moderator).** MIDJA and MIDUS participants were classified as representing Tokyo culture or United States culture, respectively. A dummy variable was constructed such that those from Tokyo were coded as 0 and those from the United States as 1.

**Trait independence and interdependence (moderator).** A 7-item independence scale ( $\alpha=0.67$ ) and a 10-item interdependence scale ( $\alpha=0.71$ ) were used, based on items from the 24-item Self-Constraint Scale, which demonstrates satisfactory validity and reliability (Singelis, 1994). A higher score on the independence scale indicates higher trait independence, and likewise for the interdependence scale.

**Psychosocial stressors (moderator).** To evaluate stress, the 10-item Perceived Stress Scale (PSS) was used ( $\alpha=0.81$ ) (Cohen et al., 1983). Higher scores indicated a higher level of psychosocial stress.

**Covariates.** Covariates were chosen based on known associations with social relationship quality, depression, or inflammation, and included the following: gender (binary), age (continuous), education level (ordinal), marital status (binary), body mass index, or BMI (continuous), number of chronic health conditions experienced in the past 12 months (continuous, participants selected which they experienced from 30 conditions such as asthma, sleeping problems, and migraines), and current smoking status (binary). All covariates were assessed at baseline, except for age, marital status in Tokyo, and BMI in Tokyo, which were assessed at their respective biomarker timepoints. All models were run with covariates.

## Data analysis

**Main analyses.** Multivariable regression was used to test each of our hypotheses. To examine whether culture moderates the link between social relationship quality and each of the three outcomes (depressive symptoms, CRP, and IL-6), social relationship quality, culture, and the interaction between the two were entered into linear models. We employed a linear combination method to find the  $p$ -values of the United States coefficients.

We then examined whether trait interdependence, trait independence, and psychosocial stressors moderate the extent to which social relationship quality predicts depressive symptoms in the United States and Tokyo. Social relationship quality, the moderator, and the interaction between social relationship quality and the moderator were entered into culture-specific models for each moderator. The dataset and R Script used to conduct the main analyses are available online at <https://www.openicpsr.org/openicpsr/project/121261/version/V1/view>.

**Sensitivity and additional analyses.** We conducted ten sensitivity and additional analyses, presented as online resources. To test the robustness of our analyses, we conducted four sensitivity analyses. First, to address missing data, we performed multiple imputations on the Tokyo dataset, the United States dataset, and the combined dataset using Gibbs sampling, creating five imputed datasets for each sample. We then calculated pooled estimates using Rubin's combination rules (Barnard & Rubin, 1999). Second, because the United States dataset contained a subpopulation of twins and siblings, we re-ran analyses containing United States data with adjustment for clustering based on family membership. Third, we re-ran the main analyses with the subset of participants with at most 2 years between predictor and outcome data collection (all 273 Tokyo participants and 495 United States participants). Fourth, we re-ran the main inflammation analyses with scores equal to or greater than 10  $\mu\text{g/mL}$  dropped from the CRP variable and scores equal to or greater than 10  $\text{pg/mL}$  dropped from the IL-6 variable. These are presented in online resources 1–4.

Next, we ran six additional analyses. The first examines whether stressors, independence, and interdependence predict depressive symptoms. The second examines the link between social relationship quality and depressive symptoms in subsets separated by participants' levels of psychosocial stressors. The third replicates all main analyses without covariates. In the fourth, survey items on spouse/partner relationship quality are included in the social relationship quality variable for subjects with a spouse or partner ( $n=805$  in the United States and  $n=220$  in Tokyo). The spouse/partner support and strain scales were identical to the family and friend support and strain scales, except for two additional questions about opening up to and relaxing with one's spouse/partner. Fifth, we separated the social relationship quality measure into positive (social support) and negative (social strain) components, examining the association of each with the outcomes. Sixth, we ran the main analyses separately for friend relationship quality, family relationship quality, and spouse/partner relationship quality. These are presented in online resources 5–10.

In all analyses, the significance level was set at  $p < .05$ , and tests were two-tailed. Robust standard errors were used across all regression analyses to deal with heteroscedasticity (Croux et al., 2003), and all predictors except for binary and moderator variables were centered around the mean. Analyses were performed in the computing programs Stata 13 (StataCorp, 2013) and RStudio (R Core Team, 2015). Data imputation was performed in RStudio using the "mice" package (R Core Team, 2015; van Buuren & Groothuis-Oudshoorn, 2011). The study was approved through the Portland Veterans Affairs Health Care System IRB.

## Results

Table 1 provides descriptive information about the 1,327 participants from the United States and Tokyo, Japan.

**Table 1.** Descriptive characteristics of participants ( $N = 1,327$ ) from Tokyo, Japan and the United States.

Variable	Japan (MIDJA) $N = 273$ $n$ (%) or $m \pm SD$	United States (MIDUS) $N = 1,054$ $n$ (%) or $m \pm SD$	$p$ -value
<b>Demographics</b>			
Male gender	115 (42.1%)	477 (45.3%)	.354
Age at biomarker assessment	$56.4 \pm 14.11$	$58.0 \pm 11.62$	.053
Race (white)	Data not collected	978 (92.8%)	
Married	199 (72.9%)	760 (72.1%)	.796
Post-secondary education	164 (60.5%)	573 (54.5%)	.076
Body mass index	$22.49 \pm 3.03$	$27.93 \pm 5.57$	<.001
Number of chronic illnesses	$2.31 \pm 2.00$	$2.30 \pm 2.38$	.968
Currently smoke cigarettes	54 (19.8%)	112 (10.6%)	<.001
<b>Predictors</b>			
Family/friend support (1–4) <sup>a</sup>	$2.60 \pm 0.51$	$3.43 \pm 0.52$	<.001
Family/friend relationship quality (1–4)	$2.89 \pm 0.36$	$3.25 \pm 0.39$	<.001
<b>Moderators</b>			
Interdependence scale (1–7)	$4.83 \pm 0.67$	$5.22 \pm 0.60$	<.001
Independence scale (1–7)	$4.72 \pm 0.75$	$5.18 \pm 0.80$	<.001
Perceived stress (1–50)	$26.07 \pm 6.03$	$21.68 \pm 6.16$	<.001
<b>Outcomes</b>			
Depressive symptoms (CES-D)	$9.75 \pm 7.18^b$	$8.02 \pm 7.72$	.001
IL-6 (pg/ml)	$1.69 \pm 2.30$	$2.79 \pm 2.79$	<.001
CRP ( $\mu$ g/ml)	$0.77 \pm 2.21$	$2.70 \pm 4.28$	<.001

<sup>a</sup>Score range is shown in parentheses.

<sup>b</sup>Sample size was reduced between 20 to 35 for these variables due to missingness.

Predictors were evaluated at MIDJA I (2008) and MIDUS II (2004–2006). Moderators were evaluated at MIDJA I (2008) and the MIDUS II Biomarker (2004–2009). Outcomes were evaluated at the MIDJA I Biomarker (2009–2010) and MIDUS II Biomarker (2004–2009).  $p$ -value was calculated by  $t$ -test for mean comparison or chi-squared for frequency comparison.

Comparisons between cultures revealed statistically significant differences in several characteristics. Participants from the United States, on average, had higher BMI, were less likely to smoke, and had higher levels of the inflammatory biomarkers IL-6 and CRP. Both trait independence and trait interdependence scores were higher in the United States, and perceived stress scores were higher in Tokyo.

#### *Are there differences between the United States and Tokyo in the link between social relationship quality and depressive symptoms?*

Social relationship quality was significantly negatively associated with depressive symptoms in the United States but not in Tokyo (Table 2 and Figure 2). Thus, culture was a significant moderator ( $\beta = -4.90$ ,  $SD = 57.68$ , 95% CI  $-8.10$  to  $-1.70$ ,  $t(1,241) = -3.01$ ,  $p = .003$ ).

#### *Are there differences between the United States and Tokyo in the link between social relationship quality and inflammation?*

Social relationship quality was not associated with either CRP or IL-6 levels (Table 2). Culture did not moderate the

link between social relationship quality and CRP ( $\beta = 1.16$ ,  $SD = 28.87$ , 95% CI  $-0.32$  to  $2.64$ ,  $t(1,252) = 1.53$ ,  $p = .125$ ), nor did it moderate the link between social relationship quality and IL-6 ( $\beta = 0.05$ ,  $SD = 16.12$ , 95% CI  $-0.84$  to  $0.94$ ,  $t(1,256) = 0.11$ ,  $p = .914$ ).

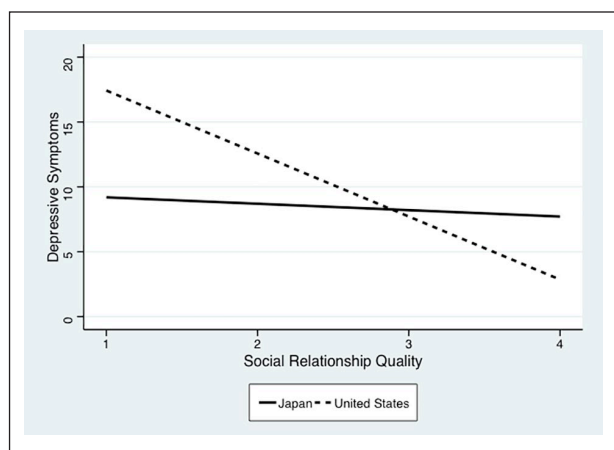
#### *Do the psychological traits of independence and interdependence moderate the link between social relationship quality and depressive symptoms in the United States and Tokyo?*

Neither trait independence nor trait interdependence moderated the connection between social relationship quality and depressive symptoms in Tokyo (independence:  $\beta = -1.35$ ,  $SD = 28.51$ , 95% CI  $-4.95$  to  $2.24$ ,  $t(233) = -0.74$ ,  $p = 0.459$ ; interdependence:  $\beta = 1.70$ ,  $SD = 23.43$ , 95% CI  $-0.13$  to  $4.65$ ,  $t(233) = 1.14$ ,  $p = 0.257$ ), although interdependence moderated the link in the United States (independence:  $\beta = 0.06$ ,  $SD = 32.05$ , 95% CI  $-1.92$  to  $2.03$ ,  $t(996) = 0.06$ ,  $p = 0.953$ ; interdependence:  $\beta = 1.88$ ,  $SD = 26.02$ , 95% CI  $0.27$  to  $3.49$ ,  $t(996) = 2.29$ ,  $p = 0.022$ ). These findings are displayed in Table 3.

**Table 2.** Cultural differences in associations between social relationship quality and depressive symptoms, C-reactive protein, and interleukin-6.

Outcome	Tokyo		United States		Cultural difference	
	b (CI)	p	b (CI)	p	b (CI)	p
Depressive symptoms	-1.25 (-4.10, 1.60) (n=245)	.390	-6.15 (-7.55, -4.75) (n=1,007)	<.001	-4.90 (-8.10, -1.70) (n=1,252)	.003
CRP	-0.89 (-2.29, 0.51) (n=266)	.213	0.27 (-0.37, 0.91) (n=997)	.408	1.16 (-0.32, 2.64) (n=1,263)	.125
IL-6	0.12 (-0.71, 0.95) (n=266)	.780	0.17 (-0.26, 0.59) (n=1,001)	.441	0.05 (-0.84, 0.94) (n=1,267)	.914

Values are based on three multiple linear regression models, one for each outcome, with an interaction between social relationship quality and culture. Each model used robust standard errors and adjusted for gender (binary), age (continuous), education level (ordinal), marital status (binary), body mass index (continuous), number of chronic health conditions (continuous), and current smoking status (binary). Model coefficients are denoted by "b." Depressive symptoms were measured with the Center for Epidemiological Studies Depression scale (CES-D); the possible range of scores was 0–60. Interleukin-6 (IL-6) was measured using blood serum and enzyme-linked immunosorbent assay (ELISA). C-Reactive Protein (CRP) was measured using blood plasma and immunonephelometry, with a sensitivity of <3 µg/mL.

**Figure 2.** Social relationship quality was more strongly linked to depressive symptoms in the United States than in Tokyo, Japan.

Associations are based on a linear multiple regression modeling the difference in the countries' associations between depressive symptoms and social relationship quality, with robust standard and no covariate adjustments. Culture moderates the association between depression and social relationship quality ( $\beta = -4.90$ ,  $p = .003$ , 95% CI  $-8.10$ – $-1.70$ ), meaning that within the United States ( $\beta = -6.15$ ,  $p < .001$ , 95% CI  $-7.55$ – $-4.75$ ) depressive symptoms decrease at a greater rate as social relationship quality increases, as compared with Tokyo ( $\beta = -1.25$ ,  $p = .390$ , 95% CI  $-4.10$ – $1.60$ ). Social relationship quality was assessed as a composite, or average, of perceived availability of emotional support and reverse-scored perceived social strain for friends and family, and partners. Depressive symptoms were measured with the Center for Epidemiological Studies Depression scale (CES-D). We created this figure in Stata 13 (StataCorp, 2013).

### Do psychosocial stressors moderate the link between social relationship quality and depressive symptoms?

Social relationship quality was found to be more protective against depressive symptoms as psychosocial stressors increase in both the United States ( $\beta = -0.39$ ,  $SD = 3.65$ , 95% CI  $-0.61$  to  $-0.16$ ,  $t(995) = -3.35$ ,  $p = .001$ ) and Tokyo ( $\beta = -0.55$ ,  $SD = 2.49$ , 95% CI  $-0.87$  to  $-0.24$ ,  $t(232) = -3.46$ ,  $p = .001$ ). These findings are displayed in Figure 3 and Table 3.

### Sensitivity analyses

Each of the four sensitivity analyses (multiple imputation for missing data, clustering for family membership, limiting participants based on the time between predictor and outcome data collection, and dropping the 2.5% of scores  $\geq 10$  µg/mL from the CRP analysis and 2.2% of scores  $\geq 10$  pg/mL from the IL-6 analysis) generally produced similar results in terms of both point estimates and significant differences.

### Additional analyses

The first analysis showed significant links between moderators and outcome variables in all cases except independence and interdependence in the Tokyo sample. The second analysis showed cultural differences in the way stressors moderate the link between social relationship quality and depressive symptoms. The third analysis, which ran the main analyses without covariates, and the fourth analysis, which included spouse/partner relationships in the social relationship quality variable, both showed generally similar results to the main models. One notable instance in which results varied was in the fifth additional analysis, which showed high perceived emotional support was associated with higher depressive symptoms in Japanese people with low perceived stress. The fifth additional analysis also revealed that culture moderated the link between social support and depression but not social strain and depression. The sixth analysis did not find strong differences between family, friend, and spouse relationship quality as they relate to outcomes. A complete compendium of additional analyses and sensitivity analyses is available online.

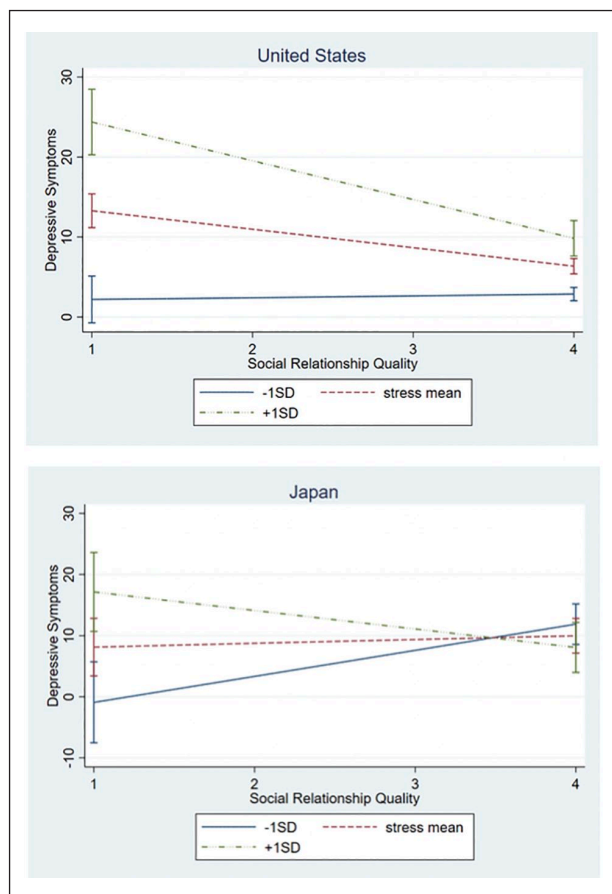
### Discussion

This longitudinal comparison of individuals living in the United States and Tokyo, Japan presents an array of results, some of which are in line with expectations and others that are rather surprising. For instance, the frequency of depression and the levels of inflammatory biomarkers are

**Table 3.** Examination of trait independence, trait interdependence, and psychosocial stressors as moderators of associations between social relationship quality and depression within Tokyo, Japan and the United States.

Trait independence	Tokyo (n = 244)	p	United States (n = 1,007)	p
Variable	b (95% CI)		b (95% CI)	
Social relationship quality	-1.33 (-4.50, 1.85)	.411	-5.65 (-7.10, -4.20)	<.001
Social relationship quality and independence interaction	-1.35 (-4.95, 2.24)	.460	0.06 (-1.92, 2.03)	.953
Trait interdependence	Tokyo (n = 244)	p	United States (n = 1,007)	p
Variable	b (95% CI)		b (95% CI)	
Social relationship quality	-1.02 (-3.66, 1.60)	.244	-6.09 (-7.48, -4.69)	<.001
Social relationship quality and interdependence interaction	1.70 (-1.25, 4.65)	.257	1.88 (0.27, 3.49)	.022
Psychosocial stressors	Tokyo (n = 243)	p	United States (n = 1,006)	p
Variable	b (95% CI)		b (95% CI)	
Social relationship quality	2.82 (0.27, 5.34)	.030	-1.96 (-3.03, 0.89)	<.001
Social relationship quality and stressors interaction	-0.55 (-0.87, -0.24)	.001	-0.39 (-0.61, -0.16)	.001

Values are based on six multiple linear regression models, one for each of the three moderators in each culture. Each model had depressive symptoms as the outcome, used robust standard errors and adjusted for gender (binary), age (continuous), education level (ordinal), marital status (binary), body mass index (continuous), number of chronic health conditions (continuous), and current smoking status (binary). Model coefficients are denoted by "b." Social relationship quality was assessed as a composite, or average, of perceived availability of emotional support and reverse-scored perceived social strain for friends and family, and partners; the possible range of scores was 1 to 4. Depressive symptoms were measured with the Center for Epidemiological Studies Depression scale (CES-D); the possible range of scores was 0–60.

**Figure 3.** Association between social relationship quality and depressive symptoms for individuals experiencing different levels of psychosocial stressors in the United States and Japan. The regression lines are for individuals experiencing three different levels of psychosocial stressors (low [mean - 1 SD], mean, and high [mean + 1 SD]). Plots are based on culture-specific multiple linear**Figure 3.** (Continued)

regression models with robust standard errors and no covariate adjustments. Social relationship quality was assessed as a composite, or average, of perceived availability of emotional support and reverse-scored perceived social strain for friends and family. Stressors were assessed using the Perceived Stress Scale; the possible range of scores was 10 to 50. Depressive symptoms were measured with the Center for Epidemiological Studies Depression scale (CES-D). We created this figure in Stata 13 (StataCorp, 2013).

consistent with prior research in similar population-based samples (Chiang et al., 2013; Nakane et al., 1991). Contrary to expectation, social relationship quality was protective against depressive symptoms in the United States but not in Tokyo. Further, social relationship quality was not associated with the inflammatory biomarkers CRP and IL-6 in either the United States or Tokyo, nor did culture moderate this association. Another surprise was that neither independence nor interdependence moderated the relation between social relationship quality and depressive symptoms. Finally, the notion that positive social relationships buffer against depressive symptoms to a greater extent as psychosocial stressors increase was supported by data from both countries.

There are several possible interpretations as to why we observed that social relationship quality was protective against depressive symptoms in the United States but not Tokyo – a result that is consistent with some studies comparing aspects of social relationship quality cross-culturally (Kim et al., 2008; Taylor et al., 2007), yet runs contrary to others (Park et al., 2013; Uchida et al., 2008). One possibility is that the traditional view that relationships influence one's self-image and well-being more in interdependent than in independent countries (Markus & Kitayama, 1991) is inaccurate, as some cultural

psychologists have argued (Matsumoto, 1999; Oyserman et al., 2002). In highly-developed modern societies, such as Tokyo, cultural tendencies around work and social life may be shifting (Chan & Lee, 2006). However, another interpretation suggested by our results is that what constitutes a high-quality social relationship differs across cultures. Indeed, research has shown that people in “interdependent” cultures such as Japan tend to seek out – and derive greater psychological benefit from – implicit and problem-focused social support, whereas those in “independent” cultures like the United States seek out and benefit more from explicit and emotion-focused support (Chen et al., 2015; Taylor et al., 2007). Finally, the observed cultural difference may also be explained by depressive symptoms’ impact on social relationship quality, as opposed to the reverse (Barger et al., 2014). In the United States, depressive symptoms may lead to greater social erosion than they would in Tokyo, where negative affect may be more accepted in relationship contexts (Curhan et al., 2014).

Although participants from the United States had, on average, higher levels of the inflammatory biomarkers IL-6 and CRP (Table 1) than participants from Tokyo, these inflammatory biomarkers were not linked to social relationship quality in either the United States or Tokyo. This finding contrasts with some prior research on the association between social relationships and IL-6 or CRP (Yang et al., 2014, 2016), but is consistent with other studies (Bajaj et al., 2016; Cassano et al., 2017; de Menezes et al., 2017). A recent review highlights additional conceptual and technical considerations regarding the use of these factors as inflammatory biomarkers and offers an expanded view of IL-6 and CRP actions – noting, for example, that some effects of IL-6 and CRP are not specifically related to inflammation and that IL-6 and CRP have both pro- and anti-inflammatory roles (Del Giudice & Gangestad, 2018). Future research might consider evaluating additional inflammatory biomarkers putatively associated with social relationship quality, such as tumor necrosis factor-alpha, C–C chemokine ligand 2, and others (Dowlati et al., 2010), thereby providing a more comprehensive assessment of inflammatory burden.

This study provides cross-cultural evidence that strong, supportive social relationships act as a buffer against depressive symptoms in times of high psychosocial stressors. However, one of the most fascinating possibilities suggested by our results is that in Tokyo, the perceived presence of emotional support may act as a sort of “double-edged sword” (Park et al., 2013): protecting against depressive symptoms when one is under high stress, but paradoxically exacerbating these symptoms in conditions of low psychosocial stress (Table 3, Figure 3, and Additional Analysis 2). The centrality of social relationships in Japanese life may make the baseline emotional

cost, or “buy-in,” of maintaining high-quality relationships greater.

Our findings should be interpreted in the context of some limitations of the study. First, the observational nature of this study prevents conclusions about the direction of causality (Barger et al., 2014). Second, despite efforts to harmonize questions across languages, it may be that the variables chosen to evaluate social relationship quality in this study are not ecologically valid across cultures, as words and concepts could take on different meanings depending on cultural context. Third, a “reference group effect” may be present, by which comparisons of individuals’ self-reports cross-culturally are confounded because what is extreme in one culture may be considered normal in another (Heine et al., 2002). This might explain the surprising consistency in mean trait independence and interdependence ratings across countries. Fourth, the ways people conceive of depression likely differs across cultures. For example, Japanese individuals diagnosed with depression report more physical complaints than Americans with depression do (Waza et al., 1999). Fifth, the United States sample had nearly four times more participants than the Tokyo sample, giving the United States analyses greater power. Sixth, the Japanese sample came only from Tokyo, but the United States sample was nationally representative and likely more culturally heterogeneous. Neither sample was an ideal representation of the culture from which it was drawn, due to size and sampling constraints. Seventh, while we conducted exploratory analyses with anti-inflammatory medication use (statins and NSAIDs) as a covariate, we did not include this covariate in our main models as we were uncertain of the medications’ anti-inflammatory effects across participants and because the medication covariate did not reach significance in any model. Eighth, inflammation comparisons were weakened by procedural differences across samples in the time of day that biomarkers were collected and the amount of fasting time before collection. Lastly, confounders are possible in any observational study; in this case, features such as socioeconomic status or sleep quality (Tomfohr et al., 2015) may have influenced results.

## Conclusion

This study indicates that social relationships are more predictive of depressive symptoms in the United States than in Tokyo, Japan. The stress moderation analysis suggests that maintaining social relationships in a collectivistic, Eastern context may incur a considerable emotional cost. These cultural differences are not explained by self-report measures of trait “independence” and “interdependence,” and social relationship quality did not predict levels of the inflammatory biomarkers CRP and IL-6 in either culture. Additional research is necessary to explore other biopsychosocial factors that might account for cross-cultural



variation in the connection between social relationships and depression.

### Author's note

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### Availability of data and material

The dataset is available at <https://www.openicpsr.org/openicpsr/project/121261/version/V1/view>. The original datasets are also publicly available at [www.midus.wisc.edu/](http://www.midus.wisc.edu/).

### Code availability

We provide the code we used to conduct the analyses in the paper at <https://www.openicpsr.org/openicpsr/project/121261/version/V1/view>.

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### Supplemental material

Supplemental material for this article is available online.

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