Social Support, Social Strain and Chronic Inflammation: Evidence from a National Longitudinal Study of U.S. Adults

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Abstract

Social relationships have long been held to have powerful effects on health and survival, but it remains unclear what the underlying biophysiological mechanism is or whether such process differs by function and domain of relationships. This study addressed gaps by examining how perceived social support and social strain from relationships with family, friends, and spouse at a prior point in time are associated with subsequent risks of chronic inflammation, as assessed by five markers (CRP, IL-6, fibrinogen, E-selectin, and ICAM-1) in a nationally representative longitudinal study of 647 adults from the Midlife Development in the United States (1995 – 2009). Results from ordinal logistic regression analysis show that (1) spouse support significantly reduced the inflammation burden; (2) family, friend, and total social strain significantly increased the inflammation burden; and (3) the negative effects of social strain were stronger than the positive effects of social support on inflammation.

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Decades of social, demographic, and epidemiologic research has firmly established the important role of social relationships and connections in shaping social and physical functioning and well-being of individuals. Social ties and support have been linked to improved mental and physical health (George et al. 1982; Cornwell & Waite 2009), a greater capacity to cope with stress (Aneshensel & Stone 1982; Thoits 2011), and increased longevity (Berkman & Syme 1979; House, Landis, and Umberson 1988). As the empirical evidence for these links continues to accrue, recent studies have increasingly attended to various social, psychological, and behavioral processes linking social relations to health (Smith and Christakis 2008; Thoits 2011; Umberson, Crosnoe, and Reczek 2010). However, important gaps exist in our knowledge of the biophysiological mechanism underlying the observed links.

First, the measures of social relations used in biosocial research are rather limited in their assessment of the quality, function, and source of social ties. Most studies have assessed the number of social ties that represent the quantitative aspect of one's social relationship (Ford et al. 2006; Loucks et al. 2006), but few have investigated the quality of such relationship as perceived by individuals. There is also a lack of understanding of how the potential mechanisms behind the links may differ by the function or source of social relationship. The vast majority of previous research has focused exclusively on the positive or stress buffering effect of social support (Orth-Gomer et al. 1993; Lyyra & Heikkinen 2006; Costanzo et al. 2005), while few studies have investigated whether strained relationships would constitute social stress that induces adverse physiological changes. It is also unclear whether different sources of social relations such as social support or strain associated with different members of one's social networks, including

family, friends, or marital partners may have differential impacts on physiological status. Second, the biophysiological mechanism underlying the observed links needs to be better elucidated. The role of innate immune dysregulation or chronic inflammation has increasingly been recognized in recent studies as a major indicator of physiological stress response that is strongly associated with some psychosocial stressors such as social isolation and perceived loneliness (Heffner et al. 2011; Steptoe et al. 2004; Yang et al. 2013). The findings, however, are limited in the selection of biomarkers (mostly to one or two such as C-reactive protein or fibrinogen). Last but not least, most previous studies are also limited in sample sizes and representativeness, and are based on cross-sectional data.

To address these gaps, the current study examined how both perceived social support and social strain from relationships with family, friends, and spouses are associated with five markers of chronic inflammation in a nationally representative longitudinal study of adults in the United States. By assessing both the positive and the negative qualities of social relationships and associating different domains of such relationships with a more comprehensive measure of inflammation over time, the current study provides unique insight into the multifaceted and dynamic links between one's social and physical worlds and contributes to the understanding of the process by which social conditions "get under the skin" to influence health.

Social Relationships and Health: Integration, Support, and Strain

Studies over the past several decades have provided overwhelming support for the notion that social relations, either defined by the quantity of individual's social network ties or the quality of relationships with others, have a significant impact on mental and physical health.

Since the seminal reviews by Cobb (1976) and Cohen & Wills (1985) that established social relationships as a significant contributor to health, various aspects of one's social relations have been linked to cognitive functioning (Seeman et al. 2001; Ertel et al. 2008), self-rated health (Cornwell & Waite 2009), incidence of cardiovascular disease (Orth-Gomer et al. 1993), all-cause mortality (Berkman & Syme 1979; Lyyra & Heikkinen 2006) and mortality from cardiovascular and malignant diseases (Penwell and Larkin 2010; Yang et al. 2013). These studies have collectively emphasized the importance of social involvement and interpersonal relationships on individual well-being. However, differences in the conceptualization and measurement of social relations across studies prohibit a direct comparison of the strengths or directions of the associations between specific aspects of social relationships with health. Some studies investigated social relations by using the number of an individual's significant social ties, the frequency of contact with social connections, and participation in social organizations and groups, thus emphasizing the role of quantitative or structural aspects of one's social network in predicting health outcomes (e.g., Berkman & Syme 1979; Ertel et al. 2008). While the links between the number of social network ties and health are strong, a count of such relationship ties is not synonymous with the quality of social relationships, as individuals can still perceive isolation despite having many social ties, while conversely, having one or several close social connections may lead to greater perceived support (Kiecolt-Glaser et al. 2010). Aligned with this qualitative conceptualization of social relationships, a number of studies have measured social relationships through individual appraisal of the quality of support received from significant members of one's social network, including perceptions of closeness, caring, and understanding from others (Lett et al. 2007; George et al. 1982; Lyyra & Heikinnen 2006). Furthermore, there is evidence that a lack of perceived support and companionship is predictive of poorer health

(Cornwell & Waite 2009). Collectively, these suggest that perceived presence of supportive relationships has the capacity to protect individuals from the adverse health outcomes associated with chronic stress, while the perceived absence of such relationships increases risk of poor health.

Beyond studies that exclusively focused on the link between social support and health, less attention has been given to the detrimental effects of relational strain on mental and physical well-being. Investigations of social strain and health have acknowledged that social connections are not explicitly positive in nature, but instead function in a balance of both benefits and costs (Walen & Lachman 2000). Studies investigating the relative contribution of social support and strain on individual well-being suggested that negative social relations represent a distinct construct from positive aspects of social networks (Finch et al. 1989; Rook 1984), emphasizing the need to assess measures of both support and strain. Furthermore, there is evidence that negative social exchanges have a more substantial impact on mental health than positive aspects of social relationships. Social strain, characterized by greater interpersonal conflict, frequent criticisms, and excessive demands from significant members of one's social network, has the potential to act as a direct source of psychosocial distress (Finch et al. 1989; Newsom et al. 2003; Newsom et al. 2005). Beyond the detrimental effects that strained social exchanges have on mental health, research has also identified negative effects of strained relationships on physical health outcomes. In particular, spousal conflict has been linked to increased risk of coronary heart disease and mortality (Eaker et al. 2007; Umberson et al. 2006).

Given the evidence above that cites the differential effects of positive and negative functions of social relationships on health, we further investigated the relative contribution of social support and strain on physiological indicators of health. Assessment of both social support

and strain expands upon prior research that links social support to better health outcomes, while also determining whether evidence implicating social strain as a more significant predictor of psychosocial distress extends to physiological outcomes. In addition to different functions that social relationship may serve, sources or domains of supportive or strained relationships from one's networks can also contribute to variations in health. For example, Mendes de Leon et al. (1999) found that the linkage between social relationships and disability in older adults varied by the type of relationship, such that the number of friend and relative contacts was significantly linked to disability and recovery, while ties with children and confidants were not associated with disability. Expanding these findings to an assessment of underlying physiological processes, our study distinguishes between three sources of social relations, including family, friends, and spouse, to assess both positive and negative functions of social relationships in relation to chronic inflammation.

Chronic Inflammation: The Biophysiological Link between Social Relationships and Health

A multitude of research has documented the association between social relationships and health and well-being; however, the physiological processes underlying the association have yet to be elucidated. One area of growing interest is the role of chronic inflammation in linking social factors to physical health outcomes. Chronic inflammation has been identified as a reliable predictor of many morbidity conditions, including cardiovascular disease, diabetes, dementia, and arthritis (Ershler & Keller 2000). While acute inflammatory response to a particular pathogen or injury is a crucial part of immunity, persistent, low-grade inflammation with no clear

pathogenic target damages healthy tissues over time, therefore increasing risk for age-related chronic illnesses (McEwen 1998; Alley et al. 2008; Hwang et al. 1997).

Research across the areas of behavioral neuroscience, immunology, and epidemiology has found chronic psychosocial stress to be a strong predictor of inflammation in the absence of infection or injury. Studies have found that the physiological processes involved in the stress response (i.e., the hypothamic-pituitary-adrenal axis and the sympathetic nervous system) can act to modulate inflammatory processes, thus providing evidence of a crucial biosocial linkage between experiences of psychosocial stress and the adverse health consequences of chronic inflammation (Black & Garbutt 2002). Several studies have documented that chronic stress diminishes the ability of the immune system to respond to anti-inflammatory signals (Cohen et al. 2012; Miller et al. 2002), and others have linked particular psychosocial stressors to immune dysregulation, including socioeconomic strain (Friedman & Herd 2010) and marital distress (Kiecolt-Glaser et al. 2005).

While the link between chronic stress and inflammation has been increasingly documented, the particular aspects of social relationships that contribute to immune function have not been fully specified due to several limitations in measurement and sample design. First, the measures of social relations that are used in biosocial research are often limited to indicators of social integration. Several studies have used social network measures to provide valuable insights into the link between social integration and inflammation (Ford et al. 2006; Loucks et al. 2006) using the Berkman social network index, which summarizes the number of social ties and participations and hence represents the quantitative and structural aspect of one's social relationships. However, few studies have assessed the quality of such relationships as perceived by individuals, which would provide a deeper assessment of how the qualitative aspects of social

relationships are linked to physiological indicators of health. A few studies have identified the beneficial effects of social support on immune function (Uchino et al. 2006), but have specifically focused on the role of social support in affecting the immune function and inflammatory processes of female cancer patients (Lutgendorf et al. 2005; Costanzo et al. 2005). An investigation of whether inflammatory processes are similarly influenced by social support in a nationally representative sample is needed to determine whether this association also exists in the absence of devastating life events and the associated extreme physiological and health-related stress.

Furthermore, studies assessing the role of social relationships in affecting inflammatory processes have not investigated whether the potential mechanisms behind the links differ by the function and source of the social relationship. While the studies above found evidence for the link between social support and physiological outcomes, few studies have investigated whether poor relationship quality would constitute social stress that induces adverse physiological changes. Evidence for the link between social strain and inflammation is limited but indicates a positive correlation. In particular, interpersonal stress from romantic partners, family and friends is associated with higher CRP and IL-6 levels six months later (Kiecolt-Glaser et al. 2005), and incidence of marital conflict increased long-term production of IL-6 and tumor necrosis factor alpha (TNFα) (Miller et al. 2009). However, no studies simultaneously investigated perceptions of both social support and strain in relation to chronic inflammation. It is also unclear whether social support or strain provided by different members of one's social networks, such as family, friends, or marital partners, have differential impacts on physiological status. Studies have linked overall perceptions of social support regardless of the source of support to inflammation (Lutgendorf et al. 2005), or have focused on one type of social relationship, such as spouse

(Kiecolt-Glaser et al. 2005), but none have simultaneously assessed the role of different domains of one's social contacts in a single study.

The precise link between social relationships and inflammation also remains unclear due to the limited measures of inflammation. Chronic inflammation has increasingly been recognized as a major physiological consequence of exposures to persistent psychosocial stressors such as socioeconomic strain (Friedman & Herd 2010), marital distress (Kiecolt-Glaser et al. 2005), social isolation (Heffner et al. 2011), and perceived loneliness (Steptoe et al. 2004). However, most studies that assessed the links between social relationships and inflammation used only one or two inflammatory markers, such as C-reactive protein (CRP) or interleukin-6 (IL-6). A recent study of three different markers of inflammation in relation to social isolation suggests that they differ in relative importance, with fibrinogen being more important than CRP or serum albumin as a correlate to social isolation (Yang et al. 2013). In addition, the study found that the cumulative inflammation burden that combines all high-risk markers is much more strongly related to isolation than any individual marker alone. Therefore, the possibility that a simultaneous assessment of multiple inflammatory markers may best capture the cumulative effects of social factors on inflammation warrants further investigation.

Finally, previous studies are also limited in sample sizes and representativeness, and are often based on cross-sectional data. Studies that have assessed the link between social support and immune function have primarily investigated this relationship in individuals affected by chronic illness (Theorell et al. 1995; Costanzo et al. 2005). Further study is necessary to determine whether these biosocial links continue to be salient in a nationally representative sample. Furthermore, most studies of the link between social relations and inflammation used cross-sectional data. It thus is unclear whether assessments of relational support or strain are

indicative of present relationship quality or more long-term social relationship patterns which may bear different consequences for chronic inflammation status. Cross-sectional associations also make causal inference difficult due to the problem of reverse causation.

In light of previous studies, we hypothesize that perceptions of social support and strain over time are associated with chronic inflammation as assessed by the cumulative burden comprised of multiple inflammatory markers. While high social support is expected to reduce subsequent inflammation burden, high social strain is expected to worsen inflammation burden. Based on evidence that implicates social strain as a more significant predictor of psychosocial distress and poor health than social support, we expect to see stronger effects of social strain on inflammation. Furthermore, we expect to observe that the influence of social relationships on inflammation will differ based on three domains of social relationships (i.e., family, friend and spouse).

Data and Methods

Data source

The data come from the National Survey of the Midlife Development in the United States (MIDUS), a longitudinal and nationally-representative study of behavioral, psychological, and social factors that contribute to age-related differences in overall health and well-being. A total of 7,108 participants aged 25-74 were recruited for the original study in 1995-96 by random digit dialing, with an oversampling of twins recruited from the national twin registry (N=1,914). Of the participants in the original sample, nearly 90 percent were white and only 5 percent were black. Phone interviews and self-administered questionnaires were completed by MIDUS

participants. The second wave of data was collected 9-10 years later (2004-2006), with a mortality-adjusted retention rate of 75%.

Biological data come from the MIDUS II biomarkers study (2004-2009), which consisted of a more detailed assessment of key biological parameters indicative of physical health. Of the 1,255 eligible participants in the Biomarkers study, 1,054 participated in both survey waves as well as the Biomarkers study. The analytic sample used in this study was limited to 647 married individuals that were present in all three stages of data collection and had no missing data for variables included in the analysis.

[Table 1. about here]

Inflammation Burden index

Chronic inflammation was measured by five markers including C-reactive protein (CRP), fibrinogen, interleukin-6 (IL-6), e-selectin, and intracellular adhesion molecule 1 (ICAM-1) at wave II. For CRP, individuals were categorized as high-risk if they had CRP levels >3.0 mg/dL, which is defined in clinical practice as the cut point for immune dysregulation. Participants with CRP levels exceeding 10.0 mg/dL were excluded from analysis because CRP beyond this point is indicative of acute inflammation induced by infection or injury. Because clinical cut points have not been determined for the other four indicators of inflammation, the high-risk category for each of these inflammatory markers was defined as the top quartile. We then constructed a summary count *index of inflammation burden* as the sum of the positive indicators. To confirm that these four inflammatory indicators comprise a single indicator of chronic inflammation, we used an oblique model in a principle components analysis. Factor analysis indicated that all five inflammatory markers load onto a single factor (36.9% of the variance, Eigen value 1.84), with

loading coefficients for CRP = 0.77, fibrinogen = 0.69, IL-6 = 0.64, E-selectin = 0.38, and ICAM-1 = 0.46. Table 1 shows that inflammation burden varies from zero (34.9% of the sample) to being at high risk for all five inflammatory markers (1.4%).

Social support/strain measures

Table 1 presents descriptive statistics of all covariates in the analysis. *Perceived social support* and *social strain* from *family*, *friends*, and *spouse* were measured and constructed in MIDUS I and II. Support and strain from family and friends were each assessed using four survey items in both waves, while six survey items were used to measure spouse support and strain. Details of the survey items and variable construction can be found in the Appendix. For the social support variables, the respondent was asked how much family members, or friends, or spouse "care about you", "understand the way you feel", "how much you can rely on them", and "how much you can open up to them", with the response categories ranging from not at all (1), a little (2), some (3), to a lot (4). Spouse support scales included two additional items that ask respondents how much spouse "appreciates you" and how much "you can be yourself" around him or her. Values of social support at MIDUS I and II were then averaged to capture long-term perceptions of support from each relationship domain. *Total social support* for each wave was calculated by taking the mean of the three support scales, and total support for both waves was calculated by taking the average of the total support measured at two waves. For the social strain variables, the respondent was asked how often do family members, friends, or spouse "make too many demands on you", "criticize you", "let you down when you are counting on them", and "do they get on your nerves", with the same Likert scale response categories as above. The spouse strain scale includes additional items that ask respondents how often a spouse "argues with you"

and "makes you feel tense." Consistent with the measurement of social support, social strain variables were averaged across the two survey waves. *Total social strain* scales were also constructed similarly to total social support scales.

Covariates

We adjusted for factors that have been associated with inflammation, including demographic characteristics, socioeconomic status, health-related behaviors, and medications (Yang et al. 2013). Table 1 presents the coding and descriptive statistics for the following covariates assessed at wave I: sex, age, household income, educational attainment, BMI, current cigarette smoking, physical activity, and medications for hypertension, cholesterol, corticosteroids, and antidepressants. We also adjusted for *markers of sympathetic nervous system (SNS) activity*, including epinephrine and norepinephrine, as SNS activity as a part of the physiological stress response has been shown to modulate inflammatory processes (Black & Garbutt 2002; Hansel et al. 2010). Because data collection did not oversample for racial minorities, we did not adjust for race in our analysis.

Analytic strategy

We estimated ordinal logistic regression models to examine the associations between social support and strain assessed in wave I and wave II and subsequent risk of inflammation assessed in the Biomarker study in wave II. The analyses proceeded in three steps. First, we estimated models that included each individual domain of social support and the total support scale, respectively. Second, we estimated models that included the three domains of social strain

and the total strain scale, respectively. And finally, we estimated models that included measures of both social support and strain within each domain of relationships and for the total summary scales to assess their associations independent of each other and the relative importance of support and strain in affecting inflammation. In all analyses, we adjusted for sex and age and compared results to models that adjust for all additional covariates. All statistical analyses were performed using Stata 12.0. Analyses were not weighted due to a significant number of missing weights for participants that did not complete both the phone interview and self-administered questionnaire.

Results

Results of the first analysis displayed in Table 2 show modest protective effects of social support. In the age- and sex-adjusted models, domain-specific support and total support were all associated with decreased risk of chronic inflammation. While the decreases in inflammation risk were not statistically significant for family or friend support, spouse support was significantly lowered inflammation burden (Odds Ratio (OR) = 0.73; 95% Confidence Interval (CI), 0.53-0.99; $p<.05$). Adjusting for all other covariates diminished the association between spouse support and inflammation, suggesting that the benefits of spouse support are partly attributed to or mediated by higher SES, better health behaviors, or other factors present in good social relations.

[Table 2 about here]

Results from the second analysis in Table 3 show robust detrimental effects of social strain on inflammation burden. Adjusting for age and sex, a higher degree of family strain and

friend strain resulted in a 77% (95% CI, 1.3 – 2.4; $p<.001$) and 50% (95% CI, 1.0 – 2.2; $p<.05$) increase in the risk of inflammation, respectively. Spousal strain, on the other hand, did not appear to significantly predict inflammation. Taking all things together, total social strain had the strongest positive effect on inflammation (OR = 1.87; 95% CI, 1.3 – 2.8; $p<.01$), suggesting that the overall perceptions of relationship strain from diverse sources most drastically elevated the inflammation burden. Adjusting for all the other covariates reduced the effect coefficients, but the strong and significant risks of inflammation remained for those experiencing higher levels of family strain or total strain, suggesting that strains associated with family relations or overall relations are potentially direct contributors to chronic inflammation whose influences are independent from other known risk factors.

[Table 3. about here]

Results shown in Table 4 indicate that including both social support and social strain indicators in the models, the latter continue to be more robust predictors of chronic inflammation. In the models that adjusted for age and sex only, family strain, friend strain, and total social strain all significantly increased the inflammation burden, with respective ORs of 1.84 (95% CI, 1.3 – 2.6; $p<.001$), 1.47 (95% CI, 1.0 – 2.1; $p<.05$), and 1.80 (95% CI, 1.2 – 2.8; $p<.01$), net of social support from the corresponding domains. Of the three domains of social strain, only spouse strain did not have a significant association with inflammation. Meanwhile, social support was generally significantly related to inflammation burden when including measures of social strain. In the fully-adjusted models, family strain and total social strain remained to be significant predictors of higher inflammation burdens, with ORs of 1.60 (95% CI, 1.1 – 2.2; $p<.01$) and 1.71 (95% CI, 1.1 – 2.7; $p<.05$), respectively. These results collectively suggest that persistent social strain from several relationship sources is a risk factor for

inflammation burden, and while these effects are partially due to SES, health behaviors, and other physiological controls, family strain and total strain remain to be significant and independent predictors of inflammation after adjusting for these factors.

[Table 4. about here]

Discussion

Our analyses of the relationships between social support, social strain, and inflammation burden support the hypothesis that long-term social strain is a significant predictor of chronic inflammation in a nationally representative sample. By assessing social support and strain both independently and additively, we found that the inflammatory impact of social support is only modest, whereas the impact of social strain is more robust and remains significant after adjusting for all additional covariates. This finding is consistent with prior evidence that finds social strain to be a direct contributor to psychosocial distress that overrides the protective effect of support (Finch et al. 1989; Newsom et al. 2003; Newsom et al. 2005). Importantly, linking long-term social strain to inflammation burden suggests that the psychosocial distress resulting from strained relationships has the potential to influence underlying physiological processes tied to later health.

In assessing the specific contribution of social support and strain within each relationship domain (i.e., family, friend, and spouse), we found variations in the impact of support or strain on inflammation burden. Spouse support modestly protected against inflammation. However, this effect was attenuated after adjusting for additional covariates, suggesting that inflammation is indirectly related to spouse support through health behaviors and socioeconomic factors. In contrast to the lack of association between total social support and inflammation, social strain

showed consistently strong effects across relationship domains. Whereas the proinflammatory effects of friend strain were explained away in the fully adjusted model, those of family strain and total strain remained substantial and significant. This suggests the need for further investigations of how strain from family relations exerts its influence on inflammatory processes. While several studies have identified a significant link between family relationships and individual well-being (Parkerson et al. 1989; Walen & Lachman 2000), the reason why family strain is particularly influential to underlying inflammatory processes remains unclear. Compared to relationships with friends and even spouses, relationships with family members, including parents, children, extended family, are likely to endure across significant periods of the life course and are not based on individual selection in the way that friends and spouses are, which may make family strain particularly detrimental to health. Future studies should assess whether specific characteristics of family relations, such as the expectations placed upon individuals by family members or the duration of family relationships, make family relations a more powerful predictor of underlying physiological processes.

Surprisingly, spousal strain was not found to have a significant and direct impact on inflammation, although evidence from other studies implicates spousal conflict as a predictor of inflammation, health, and overall well-being (Eaker et al. 2007; Kiecolt-Glaser et al. 2005; Walen & Lachman 2000). There are several potential reasons for this discrepancy. First, our study focused on chronic rather than acute inflammation. While prior studies have used acute inflammatory response immediately after physiological challenge, such as wound healing, as an indicator of immune function (Kiecolt-Glaser et al. 2005), our assessment focused on multiple physiological indicators of chronic inflammation in the absence of induced physiological stress. This suggests that chronic and acute inflammation may be differentially influenced by social

relationships. Furthermore, we used subjective perceptions of relationship quality rather than assessments of recent interactions within the relationship. It is possible that overall perceptions of relational strain, which capture broader longitudinal appraisals of relationship dynamics, measure a concept that is distinct from recollections of specific relationship events. Finally, the significance of spousal relations on inflammatory function might be dependent on the availability and reliance on other relationship sources. While our study did not assess spousal relations net of family and friend relationship quality, it is possible that spousal relations are most influential for those lacking support from other relationship domains. Future analysis of the importance of family, friend, and spouse relationships relative to one another will help to clarify their relative importance.

Our study of social relations and inflammation improved previous research in several ways. First, we used qualitative assessments of relationships rather than summary measures of social integration and network participation. This allowed for a deeper investigation of the benefits and costs of social relationships that cannot be assessed through quantitative relationship measures. Second, our measure of inflammation burden included five indicators of inflammation. Simultaneous evaluation of multiple inflammatory markers reveals the cumulative effects of social relations on broader inflammatory functioning rather than focusing on a select few markers. Finally, we used a longitudinal, nationally-representative sample to assess how social relationships across a ten year span are linked to outcomes in inflammation, thus capturing the effects of more persistent support and strain rather than cross-sectional associations.

Our analysis has several limitations that should be addressed in future studies. First, while our assessment of longitudinal data improves upon cross-sectional designs, we cannot infer a causal mechanism because it is possible that the link between social strain and inflammation is

confounded by additional factors. One confounder of particular concern is health status, since physical and mental health may influence how an individual perceives and relies on social relationships, while also having an influence on inflammation. While we observed a clear link between longitudinal perceptions of relationship quality and subsequent inflammation burden, the interrelation between social, psychological, and physiological factors is difficult to disentangle, even with a longitudinal study design, because of the limited number of waves for which these variables were available. Second, biological measurements were only made at one time point, meaning that we could not assess the simultaneous or lagged change of social relations and physiological state across time. Future availability of longitudinal data incorporating repeated measures of both social and biological measures will allow for a more thorough assessment of these biosocial linkages.

It is also possible that the effect of relationship quality on inflammation burden varies by sex, age, and the frequency in which individuals have contact with family, friends, and spouses. Evidence has suggested that females are more likely to utilize and benefit from social support than males (Kendler et al. 2005; Taylor et al. 2000), suggesting that the physiological effects of social relationships may differ by sex. Research has also supported the notion that the function of social relationships differs across the life course, as the amount of social support given and received by individuals has been found to have different effects on well-being by age (Keyes 2002). To address these potential moderating effects, we conducted additional analyses on sex- and age-stratified subsamples and found no significant differences in the link between social relationships and inflammation by sex or age group (data not shown). Further analysis also found no moderating effect of the frequency of contact with friends and family, suggesting that the

perceived quality of relationships may be a more substantial predictor of inflammatory processes than the frequency of social interaction.

Based on our findings, future studies assessing the physiological effects of social ties should consider qualitative aspects of these relationships. Furthermore, the effect of social relations on chronic inflammation appears to differ by the function of the relationship, emphasizing the importance of conceptualizing social support and social strain as fundamentally distinct predictors of inflammation burden. Social relations also have differential effects on inflammation burden depending on whether family, friends, or marital partners are the source of support or strain. Finally, this study illuminates the importance of assessing the physiological effects of social relations using a longitudinal design, thus capturing the cumulative effect of long-term relationship quality. Future investigations using longitudinal measures of both social and biological processes will help to elucidate the complex ties between social relationships and underlying physiological contributors to health and illness.

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Table 1. Sample Characteristics and Descriptive Statistics (N=647): MIDUS 1995 – 2009

Variables	Mean/% (SD)	Min	Max
Inflammatory markers (2004-2009)			
C-reactive protein (mg/dL)	2.13 (2.2)	0.14	9.98
Fibrinogen (mg/dL)	336.36 (79.07)	94.00	759.00
Interleukin-6 (pg/mL)	2.57 (2.5)	0.16	23.00
E-selectin (ng/mL)	41.15 (21.0)	0.09	161.85
ICAM-1 (ng/mL)	285.25 (97.10)	74.45	896.47
Inflammation burden index	1.23 (1.2)	0	5
0	34.9%		
1	30.0%		
2	18.9%		
3	10.5%		
4	4.3%		
5	1.4%		
Social support (1995 - 2006)			
Family support	3.53 (0.49)	1.50	4
Friend support	3.30 (0.56)	1.13	4
Spouse support	3.63 (0.45)	1.58	4
Total support	3.47 (0.42)	2	4
Social strain (1995 - 2006)			
Family strain	2.02 (0.49)	1	3.75
Friend strain	1.83 (0.39)	1	3.13
Spouse strain	2.17 (0.53)	1	3.92
Total strain	2.01 (0.36)	1.08	3.53
Neuroendocrine markers (2004-9)			
Epinephrine (ug/dL)	0.14 (0.1)	0.01	1.00
Norepinephrine (ug/dL)	1.99 (1.5)	0.23	14.30
Sociodemographic Status(2004-6)			
Female	0.50 (0.5)	0	1
Age	55.42 (11.3)	34	83
Household income (thousands)	87.46 (63.7)	0	300
Educational attainment			
High school or less	27.7%		
Some college	27.8%		
College or more	44.5%		

Health indicators(2004-9)			
Body Mass Index (BMI)	29.02 (5.6)	14.99	57.40
Current smoker	0.10 (0.3)	0	1
Exercise at least 3x a week	0.81 (0.4)	0	1
Medications(2004-9)			
Blood pressure	0.37 (0.4)	0	1
Cholesterol	0.32 (0.5)	0	1
Corticosteroids	0.12 (0.3)	0	1
Antidepressants	0.13 (0.3)	0	1

Table 2. The Effects of Social Support on Inflammation Burden: Odds Ratios (OR) with 95% Confidence Intervals (CI)

	Family Support	**Friend Support**	**Spouse Support**	**Total Support**
Age- and sex-adjusted	0.90	0.87	0.73**	0.76
	(0.68 - 1.20)	(0.67 - 1.12)	(0.53 - 0.99)	(0.54 - 1.06)
Fully-adjusted[a]	1.16	1.15	0.89	1.09
	(0.85 - 1.57)	(0.88 - 1.50)	(0.64 - 1.23)	(0.77 - 1.56)

*** p<0.01, ** p<0.05, * p<0.1; two-tailed test

[a] controls for age, sex, SNS activity (epinephrine and norepinephrine levels), household income, education, BMI, current smoking status, and medications

Table 3. The Effects of Social Strain on Inflammation Burden: Odds Ratios (OR) with 95% Confidence Intervals (CI)

	Family Strain	**Friend Strain**	**Spouse Strain**	**Total Strain**
Age- and sex-adjusted	1.77***	1.50**	1.20	1.87***
	(1.30 - 2.40)	(1.04 - 2.16)	(0.93 - 1.57)	(1.25 - 2.79)
Fully-adjusted[a]	1.44**	1.32	1.14	1.52*
	(1.05 - 1.99)	(0.91 - 1.93)	(0.86 - 1.49)	(0.99 - 2.30)

*** p<0.01, ** p<0.05, * p<0.1; two-tailed test

[a] controls for age, sex, SNS activity (epinephrine and norepinephrine levels), household income, education, BMI, current smoking status, and medications

Table 4. The Effects of Social Support and Social Strain on Inflammation Burden: Odds Ratios (OR) with 95% Confidence Intervals (CI)

	Family Relations	Friend Relations	Spouse Relations	Total
Age- and sex-adjusted				
Support	1.11	0.90	0.73	0.93
	(0.81 - 1.50)	(0.70 - 1.16)	(0.47 - 1.12)	(0.64 - 1.34)
Strain	1.84***	1.47**	1.00	1.80***
	(1.32 - 2.56)	(1.02 - 2.12)	(0.70 - 1.44)	(1.16 - 2.79)
Fully-adjusted[a]				
Support	1.34	1.19	0.98	1.30
	(0.97 - 1.84)	(0.91 - 1.55)	(0.62 - 1.54)	(0.89 - 1.91)
Strain	1.60***	1.37	1.12	1.71**
	(1.14 - 2.24)	(0.94 - 2.00)	(0.77 - 1.63)	(1.09 - 2.68)

*** p<0.01, ** p<0.05, * p<0.1; two-tailed test

[a] controls for age, sex, SNS activity (epinephrine and norepinephrine levels), household income, education, BMI, current smoking status, and medications