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Social Support and Health: A Review of Physiological Processes Potentially Underlying Links to Disease Outcomes

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Social support has been reliably related to lower rates of morbidity and mortality. An important issue concerns the physiological mechanisms by which support influences such health endpoints. In this review, I examine evidence linking social support to changes in cardiovascular, neuroendocrine, and immune function. Consistent with epidemiological evidence, social support appears to be related to more positive "biological profiles" across these disease-relevant systems. Recent research on immune-mediated inflammatory processes is also starting to provide data on more integrative physiological mechanisms potentially linking social support to health. The implications of these links, along with future research directions are discussed.

KEY WORDS: social support; physical health; cardiovascular function; neuroendocrine function; immune function; inflammation.

> "Adequate tests of the hypothesis that social circumstances alter general susceptibility to disease in humans will not be possible, however, until data are available on physiologic mechanisms capable of mediating the relationship between social events and disease outcomes." (Berkman and Syme, 1979, p. 203).

In 1979, Berkman and Syme published the results of their seminal study linking social relationships to mortality. These researchers linked questions about the extent of peoples' social connections to overall mortality and found that people who were less socially integrated had higher mortality rates. This paper was influential because it was able to rule out possible alternative explanations (e.g., results due to poorer initial health status) and hence provided the most compelling empirical links at the time between social relationships and mortality. Subsequent research has confirmed the reliable links between social support and better physical health outcomes (see reviews by Berkman *et al.*, 2000; Cohen, 1988; House *et al.*, 1988; Seeman, 1996; Uchino, 2004). Epidemiological studies indicate that individuals with low levels of social support have higher mortality rates; especially from cardiovascular disease (Berkman *et al.*, 1992; Brummett *et al.*, 2001; Frasure-Smith *et al.*, 2000; Kaplan *et al.*, 1988; Orth-Gomer *et al.*, 1993; Rutledge *et al.*, 2004; Williams *et al.*, 1992). However, there is also preliminary evidence linking support to lower cancer (Ell *et al.*, 1992; Hibbard and Pope, 1993; Welin *et al.*, 1992), and infectious disease (Lee and Rotheram-Borus, 2001; Patterson *et al.*, 1996) mortality.

Studies linking relationships to disease mortality represent the first wave of research on social support and health. The second wave must address a question of critical importance: what are the mechanisms by which social support influences such health outcomes? As noted by Berkman and Syme (1979), a mechanism of particular importance concerns the biological pathways potentially linking social support to health outcomes. Such data are important in efforts to (a) test the biological plausibility of the

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proposed links, (b) refine existing conceptual models, and (c) design appropriate interventions that consider the complexity of these links.

In this review, I will outline the main physiological pathways potentially linking social support to physical health. Social support is usually defined to include both the structure of an individual's social life (e.g., group memberships, existence of familial ties) and the more explicit functions they may serve (e.g., emotional support; see Cohen *et al.*, 2000 for a review). I will focus on research examining these measures of social support to cardiovascular, neuroendocrine, and immune function as these are the major biological systems thought to influence disease risk. In order to place this research in its proper context, I first review major pathways by which social support may influence health at different levels of analysis.

How Does Social Support Influence Physical Health Outcomes?

The structure and functions associated with our relationships provide insight into how social support may influence disease processes. Depicted in Fig. 1 is a broad model based on different theoretical perspectives (Berkman *et al.*, 2000; Cohen, 1988; Gore, 1981; Lin, 1986; Thoits, 1995; Umberson, 1987) and the available literature linking social support to physical health (see Uchino, 2004 for more detail). Accordingly, structural and functional measures of support may ultimately influence morbidity and mortality through two distinct but not necessarily independent pathways. One pathway involves behavioral processes including health behaviors and adherence to medical regimens as outlined by social control and social identity theorists (Lewis and Rook, 1999; Umberson, 1987). According to this view, social support is health-promoting because it facilitates healthier behaviors such as exercise, eating right, and not smoking; as well as greater adherence to medical regimens. This can happen in a direct (e.g., health-related informational support) or indirect (e.g., life meaning) manner (DiMatteo, 2004; Lewis and Rook, 1999; Umberson, 1987). In fact, health behaviors are one of the few variables that appear to explain at least part of the variance between social support and mortality (e.g., Kaplan *et al.*, 1994). Of course, not all "supportive" relationships encourage healthier behaviors. Network ties can set a negative example and/or promote risky health behaviors

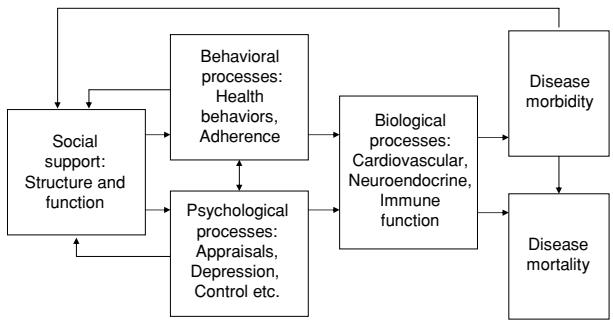

Fig. 1. Broad model highlighting potential pathways linking social support to physical health.

(see reviews by Burg and Seeman, 1994; Wills and Yaeger, 2003). We will return to this complexity in social support processes later in the review.

The other major pathway involves psychological processes that are linked to appraisals, emotions or moods (e.g., depression), and feelings of control (Cohen, 1988; Gore, 1981; Lin, 1986). There is strong evidence linking social support to these psychological processes (Barrera, 2000), although direct evidence for their mediational role on health outcomes is lacking (House, 2001). Note that the behavioral and psychological levels are linked as each has been shown to exert an influence over the other. For instance, feelings of stress can adversely impact the practice of health behaviors (e.g., Ng and Jeffery, 2003) while health behaviors such as exercise can have beneficial effects on feelings of stress (e.g., Rejeski *et al.*, 1992). Finally, these psychological and behavioral pathways may have reciprocal influence on social support processes. For instance, psychological distress may influence perceptions of support and contribute to negative social interactions (Alferi *et al.*, 2001; Coyne, 1976).

An additionally important aspect of the model concerns the proposed links to and from disease morbidity. This makes salient two aspects of this broad model. First, the links with morbidity highlight the potential role of social support in the development of certain diseases. Second, the feedback loop between morbidity and social support highlights the unique challenges faced by individuals diagnosed with disease that can impact their social network. Close network members are often called upon as sources of support after the diagnosis of disease (Bolger *et al.*, 1996). In some cases, the strain may result in network members withdrawing in an attempt to cope with an overwhelming situation (Bolger *et al.*, 1996). In other

cases, stressful situations can provide an opportunity for growth in personal relationships (Holahan and Moos, 1990).

Of central importance to this review is that the links between social support and disease are hypothesized to be mediated through relevant physiological processes; including changes in cardiovascular, neuroendocrine, and immune function (Berkman *et al.*, 2000; Uchino *et al.*, 1996). I first start my review by examining the links between social support and health-relevant cardiovascular alterations, followed by relevant research on neuroendocrine and immune function. Finally, a focus on more integrative biological mechanisms is outlined by highlighting recent research on immune-mediated inflammatory processes.

Social Support and Cardiovascular Function

Most of the evidence linking social support to biological pathways has examined the cardiovascular system (Uchino *et al.*, 1996). There is strong evidence linking social support to aspects of cardiovascular function that may confer lower risk for disease (Uchino, 2004). One of these paradigms includes conceptual links to the reactivity hypothesis of disease (Lepore, 1998). According to this perspective, individuals or situations characterized by high levels of cardiovascular reactivity (usually indexed by blood pressure or heart rate) may be related to higher risk for the development and exacerbation of cardiovascular disease. Research linking reactivity to cardiovascular disease is still on-going, but current evidence is consistent with this hypothesis (Treiber *et al.*, 2003). Social support may thus be beneficial because it "buffers" the potentially harmful influences of stress-induced cardiovascular reactivity (Cohen and Wills, 1985).

In an early study testing this hypothesis, Kamarck *et al.* (1990) found that the presence of a friend was associated with lower blood pressure reactivity to an acute psychological stressor (i.e., mental arithmetic). Subsequent research has revealed complex associations as a function of such mere presence paradigms (Uchino *et al.*, 1996). For instance, the simple presence of a friend may increase evaluation apprehension and interfere with support processes (Allen *et al.*, 1991). Studies that directly manipulate the supportive function of relationships through verbal support appear to provide more consistent evidence for this stress-buffering hypothesis (Gerin *et al.*, 1992; Lepore, 1995; Thorsteinnsson *et al.*, 1998; see review by Thorsteinnsson and James, 1999).

There are several important assumptions in these laboratory reactivity studies of social support that deserve mention in predicting the development of cardiovascular disease. These studies assume that this buffering process would occur outside of the laboratory over relatively long periods of time, to reduce the potentially harmful increases in cardiovascular reactivity associated with stressful life events. I know of no such longitudinal test of these associations. However, if these assumptions are correct, one would expect for the effects of social support to be more evident in older individuals due to the cumulative influence of social support across the years. To date, we have provided evidence in several studies showing that social support is associated with lower resting blood pressure primarily in older adults (Uchino *et al.*, 1995; Uchino *et al.*, 1999; also see Ong and Allaire, 2005).

Social support may also be beneficial because it is associated with lower blood pressure during everyday life. This would be an important conceptual link because studies examining the prognostic value of ambulatory blood pressure suggest that it predicts future cardiovascular problems above and beyond that predicted by conventional (resting) blood pressure readings (e.g., Perloff *et al.*, 1983). Existing studies are consistent with a link between social support and lower ambulatory blood pressure (Gump *et al.*, 2001; Linden *et al.*, 1993; Spitzer *et al.*, 1992; Steptoe *et al.*, 2000). In one illustrative study, Steptoe and colleagues (2000) found that when the role of being a parent was combined with high levels of functional support it predicted the greatest evening reduction in ambulatory systolic blood pressure compared to any of these measures in isolation. These ambulatory studies are consistent with the role of social support as a risk-reducing factor in the development of cardiovascular disease (also see Horsten *et al.*, 1999). In future research, ambulatory protocols might also be designed to model the stress-buffering effects of support previously examined in laboratory reactivity paradigms.

More direct evidence for a role of social support on the development of cardiovascular disease can be found in recent data utilizing imaging techniques. To date, several of these studies have shown that social support predicts less underlying atherosclerosis (Angerer *et al.*, 2000; Knox *et al.*, 2000; Seeman and Syme, 1987; Kop *et al.*, 2005; Wang *et al.*, 2005). For instance, the National Heart, Lung, and Blood

Institute Family Heart Study examined links between social support and carotid artery atherosclerosis using B-mode ultrasonic imaging (Knox *et al.*, 2000). Results of this study revealed that social support was related to less underlying atherosclerosis in women at high risk for the development of heart disease.

It is also important to note that social support appears to play a role in the progression of diagnosed cardiovascular disease (Berkman *et al.*, 1992; Brummett *et al.*, 2001). One potential mechanism for this action is through the stress-buffering properties of social support. Acute stress in cardiac patients may precipitate ischemia due to hemodynamic changes in blood pressure (Rozanski *et al.*, 1988). Thus, social support may be beneficial to cardiac patients because it decreases deleterious cardiovascular changes during stress. Imaging studies are also consistent with the possibility that social support influences the progression of clinical cardiovascular disease. Women with established coronary artery disease who were low in emotional support had faster disease progression as indexed by angiography over a subsequent three year period (Wang *et al.*, 2005; also see Angerer *et al.*, 2000). However, a stronger test of the above physiological pathways (as well as those detailed below) would require conceptual modeling to test if these parameters directly mediated epidemiological links between social support and disease outcomes.

Social Support and Neuroendocrine Function

In comparison to cardiovascular function, there is relatively little research linking social support to neuroendocrine function (Uchino *et al.*, 1996). As a result, conclusions regarding such links should be considered tentative. The relative lack of such data is noteworthy because hormones and neurotransmitters mediate aspects of cardiovascular and immune function (Ader *et al.*, 2001) and thus may shed light on how these diverse physiological systems are coordinated as a function of social support. There is some evidence that social support is associated with lower plasma and urinary catecholamine levels (Fleming *et al.*, 1982; Seeman *et al.*, 1994; Grewen *et al.*, 2005). These associations are consistent with the beneficial effects of social support on cardiovascular function.

Another important hormone implicated in disease processes is cortisol which has well-documented immunosuppressive effects (Greenspan and Baxter, 1994). Potential associations between social support and cortisol may be especially important for cancer patients as the immune system is thought to be the primary mechanism of defense against malignant diseases (Dunn *et al.*, 2002). In our earlier review, we found little evidence for a link between social support and cortisol levels (Uchino *et al.*, 1996). Many of these early studies utilized only one plasma cortisol assessment (usually in the morning) so we speculated that advances in the measurement of cortisol may be needed to detect such an association. Turner-Cobb and colleagues (2000) utilized a more comprehensive protocol by measuring salivary cortisol over the course of three days in breast cancer patients. Results showed that social support predicted lower overall cortisol levels (Turner-Cobb *et al.*, 2000; also see Heinrichs *et al.*, 2003). In general, studies that have measured salivary cortisol over several time points have found more consistent links to social support (Heinrichs *et al.*, 2003; Milagros *et al.*, 2004; Turner-Cobb *et al.*, 2000; but see Olga and Steptoe, 2001).

There are additional neuroendocrine processes that require increased attention in social support studies. For instance, opioids have links to both the cardiovascular and immune systems (Carr *et al.*, 1996; McCubbin *et al.*, 1993) although very little research has examined potential associations with social support. Another neuroendocrine hormone with promising and largely unexplored links to social support is oxytocin (Knox and Uvnas-Moberg, 1998; Taylor *et al.*, 2000). Besides its more established physiologic role (e.g., uterine contractions during labor), oxytocin has anti-stress effects in both the brain and more peripheral physiological systems (Taylor *et al.*, 2000). For instance, oxytocin release is associated with decreases in cortisol levels, blood pressure, sympathetic activity, and increases in parasympathetic activity (Uvnas-Moberg, 1998).

At present little research exists on oxytocin responses in humans and its potential link to social support. In one of the few human studies, perceptions of partner support were uniformly associated with higher oxytocin levels (Gwenen *et al.*, 2005). It is also possible that oxytocin may be a primary pathway regulating the stress-buffering effects of social support on other physiological systems (Knox and Uvnas-Moberg, 1998). This hypothesis was tested by Heinrichs and colleagues (2003) who manipulated social support (via a friend) and oxytocin levels (via a nasal spray) in men undergoing acute psychological stress. Consistent with the stress-buffering hypothesis, social support was associated with lower cortisol responses. However, these support effects were

especially evident if combined with the oxytocin manipulation as such individuals showed the smallest increases in cortisol during stress. These studies suggest that additional research on this and related neuroendocrine hormones may provide novel insight into biologic processes mediating social support effects.

Social Support and Immune Function

A final physiological pathway by which social support may influence physical health is via the immune system. Indeed, some of the strongest associations we found in our earlier meta-analytic review were for a link between social support and better immune function, especially in older adults (Uchino *et al.*, 1996). This association is particularly noteworthy because the risk of cancer increases with age and infectious diseases are a leading cause of death in older individuals (Effros and Walford, 1987).

A number of recent studies continue to suggest that social support is related to better immune function (Dixon *et al.*, 2001; Esterling *et al.*, 1996; Lutgendorf *et al.*, 2005; Miyazaki *et al.*, 2005). Of particular note are studies that have examined the link between social support and natural killer cell activity (e.g., Esterling *et al.*, 1996; Lutgendorf *et al.*, 2005) because natural killer cells are thought to play an important "surveillance" role in cancer (Abbas and Lichtman, 2003). This association was tested by Lutgendorf and colleagues (2005) in ovarian cancer patients. Replicating prior research (Levy *et al.*, 1990), results showed that social support predicted greater natural killer cell activity in peripheral blood. Importantly, natural killer cell activity in tumor-infiltrating lymphocytes was also greater for individuals with high levels of social support.

Another patient population of importance given links between social support and immune function is HIV+ individuals. A few studies have reported an association between social support and helper T-cell counts in HIV+ men (Persson *et al.*, 1994; Theorell *et al.*, 1995). In one long-term study, researchers examined this link across a five year period (Theorell *et al.*, 1995). Results showed that social support became a more powerful predictor of helper T-cells as time progressed (years four and five). For instance, during year five of the study, individuals with high social support showed a -37% change in helper T-cells compared to a -64% change in helper T-cells for individuals low in support. However, several studies have failed to find an association between social support and aspects of immune function in HIV+ men (Goodkin *et al.*, 1992; Perry *et al.*, 1992). The state of this literature makes firm conclusions difficult, but suggests potential moderators may need greater attention in future studies.

It is also important to note that existing research is consistent with the biological significance of the links between social support and immunity. For instance, individuals lower in support were less likely to clinically seroconvert to a Hepatitus B vaccination (Glaser *et al.*, 1992). Social support has also been correlated with antibody titers following influenza vaccination (Moynihan *et al.*, 2004; Pressman *et al.*, 2005). These results are consistent with data by Cohen *et al.* (1997) who found that individuals with more diverse social networks (i.e., relationships from a variety of domains such as work, home, church) were less likely to develop clinical colds following inoculation.

Integrative Mechanisms: Social Support and Immune-Mediated Inflammation

Consistent with epidemiological findings, much of the research conducted above suggests a role for social support across a number of diseases (i.e., cardiovascular disorders, cancer, infectious diseases). As a result, research that examines more integrative mechanisms can provide a basis for understanding the general health risks associated with poor social support. Recent research on immune-mediated inflammation provides one possible avenue for a more integrative approach. Traditionally, immune processes have been linked to infectious diseases and cancer. Cardiovascular disease can now be added to that list of disease processes with an immunologic component (Libby, 2002; Ross, 1999).

Immune processes are implicated in just about every stage of atherosclerosis (Libby, 2002). One of the earliest events in the atherogenic process is endothelial damage (Ross, 1999). At early stages of damage, the endothelium begins to express adhesion molecules such as vascular adhesion molecule-1 that help in the binding of immune cells to the vasculature. Monocytes and T-lymphocytes are then recruited to sites of inflammation and migrate into vessel walls via various cytokines/chemokines (e.g., monocyte chemoattractant protein-1) that are released from vascular cell walls (Charo and Taubman, 2004). Once inside vessel walls, these immune cells proliferate and release a variety of growth factors (e.g., platelet-derived growth factors) and

cytokines (e.g., interleukin-1) characteristic of the inflammatory response (Libby, 2002). Immune events at later stages can lead to the rupture of such plaques. For instance, macrophages are common in vulnerable plaques and can produce enzymes (e.g., metalloproteinases) that degrade the fibrous cap, while T-lymphocytes release interferon-γ that can impede collagen formation by smooth muscle cells (Libby, 2002).

Importantly, there are preliminary data linking social support to immune-mediated inflammatory processes. One cytokine of recent interest is interleukin-6 given its diverse physiologic role in inflammation as well as the adaptive immune response (Hawkley *et al.*, in press; Kiecolt-Glaser *et al.*, 2002). For instance, interleukin-6 is a potent stimulator of C-reactive protein and fibrinogen production from the liver (Libby, 2002). To date, three studies found that social support was related to lower levels of interleukin-6 (Costanzo *et al.*, 2005; Friedman *et al.*, 2005; Lutgendorf *et al.*, 2000). Kiecolt-Glaser and colleagues (2005) also found in a laboratory study that supportive interactions were associated with a *stronger* acute increase in inflammatory cytokines (tumor necrosis factor-α, interleukin-1, interleukin-6) at the site of blister wounds, as well as faster wound healing compared to a conflict interaction. This study highlights the importance of considering the disease context and time course (e.g., acute versus more chronic inflammation) in links between social support and disease processes.

Despite these preliminary and promising links, there are several complexities in examining inflammatory processes that require discussion (Hawkley *et al.*, in press). First, cytokines can activate many different cell types and hence are associated with diverse biologic effects (Abbas and Lichtman, 2003). For instance, although evidence does exists on the pro-inflammatory influences of interleukin-6 (e.g., via induction of C-reactive protein, see Verma *et al.*, 2004); interleukin-6 also appears to have important anti-inflammatory effects (e.g., via activation of the hypothalamic-pituitary-adrenal axis, see Barton, 1997; Hawkley *et al.*, in press). As a result, Hawkley and colleagues (in press) caution researchers in interpreting the results of correlational studies because in some circumstances it is possible that elevated levels of interleukin-6 may be co-activated in an attempt to control inflammation.

A second complexity related to links between social support and inflammation that will require increased attention relates to the conditions under which normal control points can be disrupted (Hawkley *et al.*, in press). One important control mechanism is activation of the hypothalamic-pituitary-adrenal axis that tends to suppress immunity (Munck *et al.*, 1984). However, psychosocial processes such as chronic stress can also lead to a state of glucocorticoid resistance (Miller *et al.*, 2002; Hawkley *et al.*, in press). For instance, pro-inflammatory cytokines such as tumor necrosis factor-α can modulate glucocorticoid receptors on cytokine producing cells (Webster *et al.*, 2001). The cytokine macrophage migration inhibitory factor is also receiving attention as an important mechanism of glucocorticoid resistance (Baugh and Donnelly, 2003; Hawkley *et al.*, in press).

Implications and Future Directions

Researchers have long argued for the importance of understanding the biological mechanisms linking social support to physical health outcomes (Berkman and Syme, 1979; Broadhead *et al.*, 1983; Cassell, 1976). The research reviewed above represents the tremendous progress researchers have made to date in providing answers to this question. There is ample evidence linking social support to aspects of the cardiovascular, neuroendocrine, and immune system which is consistent with the beneficial role of social support across different diseases (Uchino, 2004). Recent research on immune-mediated inflammatory processes is also providing a more integrative perspective on modeling how these biological changes are coordinated in ways that lower disease risk.

Despite these promising links to health-relevant biological processes, there are several issues that will require increased attention in this literature. One issue concerns the need for more data on the stage of disease potentially impacted by social support (i.e., development and/or progression of diagnosed disease). One perspective that may be helpful in this regard is a lifespan or successful aging approach (Rowe and Kahn, 1987). This perspective highlights the importance of linking social support to disease processes throughout the lifespan; with appropriate attention to developmental processes that impact social functioning (Antonucci and Akiyama, 1987; Carstensen, 1992). For instance, there is evidence that some variance in perceptions of social support may be established early in life (Sarason *et al.*, 1986). Graves and colleagues (1998) found that

ratings of early parental closeness were associated with a greater number of close contacts providing social support, as well as increased group participation thirty years later. Such data suggest that early social processes can cast "long shadows" that become more evident from a lifespan perspective.

It is also important to keep in mind that biological mechanisms represent just one level of analysis in the complex links between relationships and physical health (see Figure 1). There is a pressing need to also identify processes and mechanisms impacting associations between social support and health at other levels of analysis. Although not depicted in Figure 1, more macro social-cultural factors can influence support-seeking as well as the effectiveness of support (Dressler, 1994; Taylor *et al.*, 2005; see Uchino, 2004). For instance, social networks are normally composed of individuals with a similar socioeconomic background (Lin, 1982). As a result, the broader social networks of individuals low in socioeconomic status may be similarly taxed and thus be limited sources of support (Krause, 2001). It is also important to note that the biological mechanisms reviewed earlier can serve as intermediate endpoints by which to examine other levels of analysis (see Figure 1). For instance, researchers can model if links between social support and ambulatory blood pressure are mediated by lower perceptions of stress. Such research can inform epidemiological studies that track social support, relevant multilevel mechanisms (including biological pathways), and disease morbidity/mortality over relatively long periods of time.

Another important consideration in my view is the need for a more comprehensive view on social relationships and health that incorporates both positive and negative features (Uchino *et al.*, 2001). It is clear that social ties may serve as significant sources of stress or become models for deviant or unhealthy behaviors (Burg and Seeman, 1994; Wills and Yaeger, 2003). Research also indicates that many of our close relationships are characterized by both helpful and upsetting qualities (Fincham and Linfield, 1997; Uchino *et al.*, 2001). In fact, the effect sizes associated with social support and health may actually be larger than it appears due to the practice of ignoring the co-occurring negative feelings that exist in many of our close relationships. Future research that takes into account this complexity in relationships can serve to inform and refine existing theoretical models of social support processes (Newsom *et al.*, 2003; Uchino *et al.*, 2001).

Of course, the application of this research to interventions should also receive priority. Several studies are consistent with the health benefits of social support in both focused (e.g., Levine *et al.*, 1979) and more general psychosocial interventions (Linden *et al.*, 1996; Rozanski *et al.*, 1999). One of the most comprehensive social support interventions to date was the multi-site Enhancing Recovery in Coronary Heart Disease (ENRICHD) clinical trial (The ENRICHD Investigators, 2003). In this intervention, myocardial infarction patients with low social support and/or depression were randomized to cognitive-behavioral therapy that individually addressed problems related to depression/social support. Results of this study revealed a statistically significant increase in social support after six months for participants given the intervention. However, after about twenty-nine months there were no differences in survival between the support and usual care groups.

The results of the ENRICHD trial were surprising in that it was inconsistent with the large body of epidemiological and clinical/laboratory studies linking support to beneficial health outcomes. Why was the support intervention not associated with differences in survival? There are a few possibilities discussed by the authors. One explanation relates to the effect size associated with the intervention (The ENRICHD Investigators, 2003). At the six month period there was approximately a 9% difference in support changes that favored the intervention. However, there was no longer a significant difference between the intervention and usual care groups at the forty-two month follow-up (due mostly to unexpected improvements in social support for the usual care group). Thus, the initial support differences may have been too small or not maintained over a long enough period of time to influence the main cardiovascular outcomes. In fact, as discussed by the authors, it is unknown how much of a change in social support may be needed or how long an intervention is necessary to influence cardiac outcomes that have a long-term etiology. It should be noted that post-hoc analyses of these data have shown beneficial influences for some patient subgroups (Burg *et al.*, 2005; Schneiderman *et al.*, 2004). Overall, the results of the ENRICHD trial highlight the challenges in translating prior social support research to interventions that attempt to modify equally complex disease processes.

The complexity in designing support interventions highlights the need to focus on a more basic question: "what is social support?" There is presently

no universally agreed upon definition of social support. In some cases it refers to aspects of the social network (groups, familial ties), at other times to specific behaviors (e.g., emotional or informational support), and sometimes to our perceived availability of support resources that may be shaped early in life. Answers to the question of "what is social support" will likely require complex analyses of childhood social experiences, personality, and close relationships over the lifespan (Badr *et al.*, 2001; Pierce *et al.*, 2000; Smith and Gallo, 2001). Such an analysis may be necessary if we are to understand the development and maintenance of strong support networks that then facilitate health-relevant psychological, behavioral, and biologic processes. Due to the complexity of these issues, an interdisciplinary perspective will be crucial, and if successful, could highlight multiple potential entry points for intervention.

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REFERENCES

Abbas, A. K., and Lichtman, A. H. (2003). *Cellular and molecular immunology* (5th edn.). Harcourt Brace and Company, Philadelphia, Pa.

Ader, R., Felton, D. L., and Cohen, N. (2001). *Psychoneuroimmunology* (3rd edn.). Academic Press, NY.

Alferi, S. M., Carver, C. S., Antoni, M. H., Weiss, S., and Duran, R. E. (2001). An exploratory study of social support, distress, and life disruption among low-income Hispanic women under treatment for early stage breast cancer. *Health Psychol.* 20: 41–46.

Allen, K. M., Blascovich, J., Tomaka, J., and Kelsey, R. M. (1991). Presence of human friends and pet dogs as moderators of autonomic responses to stress in women. *J. Pers. Soc. Psychol.* 61: 582–589.

Angerer, P., Siebert, U., Kothny, W., Muhlbauer, D., Mudra, H., and von Schacky, C. (2000). Impact of social support, cynical hostility and anger expression on progression of coronary atherosclerosis. *J. Am. Coll. Cardiol.* 36: 1781–1788.

Antonucci, T. C., and Akiyama, H. (1987). Social networks in adult life and a preliminary examination of the convoy model. *J. Gerontol.* 42: 519–527.

Badr, H., Acitelli, L., Duck, S., and Carl, W. J. (2001). Weaving social support and relationships together. In Sarason, B., and Duck, S. (Eds.), *Personal relationships: Implications for clinical and community psychology* (pp. 1–14). John Wiley and Sons Inc., West Sussex, England.

Barrera, M. Jr. (2000). Social support research in community psychology. In Rappaport, J., and Seidman, E. (Eds.), *Handbook of Community Psychology* (pp. 215–245). Kluwer Academic/Plenum Publishers, NY.

Barton, B. E. (1997). Molecule of the month: IL-6: Insights into novel biological activities. *Clin. Immunol. Immunopathol.* 85: 16–20.

Baugh, J. A., and Donnelly, S. C. (2003). Macrophage migration inhibitory factor: A neuroendocrine modulator of chronic inflammation. *J. Endocrinol.* 179: 15–23.

Berkman, L. F., Glass, T., Brissette, I., and Seeman, T. E. (2000). From social integration to health: Durkheim in the new millennium. *Soc. Sci. Med.* 51: 843–857.

Berkman, L. F., Leo-Summers, L., and Horwitz, R. I. (1992). Emotional support and survival after myorcardial infaction: A prospective, population-based study of the elderly. *Ann. Intern. Med.* 117: 1003–1009.

Berkman, L. F., and Syme, S. L. (1979). Social networks, host resistance, and mortality: A nine-year follow-up study of Alameda county residents. *Am. J. Epidemiol.* 109: 186–204.

Bolger, N., Foster, M., Vinokur, A. D., and Ng, R. (1996). Close relationships and adjustment to a life crisis: The case of breast cancer. *J. Personal. Soc. Psychol.* 70: 283–294.

Brummett, B. H., Barefoot, J. C., Siegler, I. C., Clapp-Channing, N. E., Lytle, B. L., Bosworth, H. B., Williams, R. B. Jr., and Mark, D. B. (2001). Characteristics of socially isolated patients with coronary artery disease who are at elevated risk for mortality. *Psychosom. Med.* 63: 267–272.

Broadhead, W. E., Kaplan, B. H., James, S. A., Wagner, E. H., Schoenbach, V. J., Grimson, R., Heyden, S., Tibblin, G., and Gehlbach, S. H. (1983). The epidemiological evidence for a relationship between social support and health. *Am. J. Epidemiol.* 117: 521–537.

Burg, M. M., and Seeman, T. E. (1994). Families and health: The negative side of social ties. *Ann. Behav. Med.* 16: 109–115.

Burg, M. M., Barefoot, J., Berkman, L., Catellier, D. J., Czajkowski, S., Saab, P., Huber, M., DeLillo, V., Mitchell, P., Skala, J., and Taylor, C. B. for the ENRICHD Investigators (2005). Low Perceived Social Support and Post–Myocardial Infarction Prognosis in the Enhancing Recovery in Coronary Heart Disease Clinical Trial: The Effects of Treatment. P*sychosom. Med.* 67: 879–888.

Carr, D. J. J., Rogers, T. J., and Weber, R. J. (1996). The relevance of opioids and opioid receptors on immunocompetence and immune homeostasis. *Proc. Soc. Exp. Biol. Med.* 213: 248–257.

Carstensen, L. L. (1992). Social and emotional patterns in adulthood: Support for socioemotional selectivity theory. *Psychol. Aging*. 7: 331–338.

Cassell, J. (1976). The contribution of the social environment to host resistance. *Am. J. Epidimiol.* 104: 107–123.

Charo, I. F., and Taubman, M. B. (2004). Chemokines in the pathogenesis of vascular disease. *Circ. Res.* 95: 858–866.

Cohen, S. (1988). Psychosocial models of the role of social support in the etiology of physical disease. *Health Psychol.* 7: 269–297.

Cohen, S., Doyle, W. J., Skoner, D. P., Rabin, B. S., and Gwaltney, J. M. (1997). Social ties and susceptibility to the common cold. *J. Am. Med. Assoc.* 277: 1940–1944.

Cohen, S., Underwood, L. G., and Gottlieb, B. H. (2000). *Social support measurement and intervention: A guide for health and social scientists* (pp. 53–85). Oxford University Press, NY.

Cohen, S., and Wills, T. A. (1985). Stress, social support, and the buffering hypothesis. *Psychol. Bull.* 98: 310–357.

Costanzo, E. S., Lutgendorf, S. K., Sood, A. K., Anderson, B., Sorosky, J., and Lubaroff, D. M. (2005). Psychosocial factors and interleukin-6 among women with advanced ovarian cancer. *Cancer* 104: 305–313.

Coyne, J. C. (1976). Depression and the response of others. *J. Abnorm. Psychol.* 85: 186–193.

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: A meta-analysis. *Health Psychol.* 23: 207–218.

Dixon, D., Kilbourn, K., Cruess, S., Klimas, N., Fletcher, M. A., Ironson, G., Baum, A., Schneiderman, N., and Antoni, M. H. (2001). Social support mediates the relationship between loneliness and Human Herpesvirus-Type 6 (HHV-6) antibody titers in HIV + gay men following Hurricane Andrew. *J. Appl. Soc. Psychol.* 31: 1111–1132.

Dressler, W. (1994). Cross-cultural differences and social influences in social support and cardiovascular disease. In Shumaker, S. A., and Czajkowski, S. M. (Eds.), *Social support and cardiovascular disease* (pp. 167–192). Plenum Press, NY.

Dunn, G. P., Bruce, A. T., Ikeda, H., Old, L. J., and Schreiber, R. D. (2002). Cancer immunoediting: From immunosurveillance to tumor escape. *Nature Immunol.* 3: 991–998.

Effros, R. B., and Walford, R. L. (1987). Infection and immunity in relation to aging. In Goidl, E. A. (Ed.), *Aging and the immune response* (pp. 45–65). Marcel Dekker, NY.

Ell, K., Nishimoto, R., Medianski, L., Mantell, J., and Hamovitch, M. (1992). Social relations, social support and survival among patients with cancer. *J. Psychosom. Res.* 36: 531–541.

Esterling, B. A., Kiecolt-Glaser, J. K., Glaser, R. (1996). Psychosocial modulation of cytokine-induced natural killer cell activity in older adults. *Psychosom. Med.* 58: 264–72.

Fincham, F. D., and Linfield, K. J. (1997). A new look at marital quality: Can spouses feel positive and negative about their marriages? *J. Fam. Psychol.* 11: 489–502.

Fleming, R., Baum, A., Gisriel, M. M., and Gatchel, R. J. (1982). Mediating influences of social support on stress at Three Mile Island. *J. Hum. Stress.* 8: 14–22.

Frasure-Smith, N., Lespérance, F., Gravel, G., Masson, A., Juneau, M., Talajic, M., and Bourassa, M. G. (2000). Social support, depression, and mortality during the first year after myocardial infarction. *Circulation.* 1919–1924.

Friedman, E. M., Hayney, M. S., Love, G. D., Urry, H. L., Rosenkranz, M. A., Davidson, R. J., Singer, B. H., and Ryff, C. D. (2005). Social relationships, sleep quality, and interleukin-6 in aging women. *PNAS.* 102: 18757–18762.

Gerin, W., Pieper, C., Levy, R., and Pickering, T. G. (1992). Social support in social interaction: A moderator of cardiovascular reactivity. *Psychosom. Med.* 54: 324–336.

Glaser, R., Kiecolt-Glaser, J. K., Bonneau, R., Malarkey, W., and Hughes, J. (1992). Stress-induced modulation of the immune response to recombinant hepatitis B vaccine. *Psychosom. Med.* 54: 22–29.

Goodkin, K., Blaney, N. T., Feaster, D., Fletcher, M. A., Baum, M. K., Mantero-Atienza, E., Klimas, N. G., Millon, C., Szapocznik, J., and Eisdorfer, C. (1992). Active coping style is associated with natural killer cell cytotoxicity in asymptomatic HIV-1 seropositive homosexual men. *J. Psychosom. Res.* 36: 635–650.

Gore, S. (1981). Stress-buffering functions of social supports: An appraisal and clarification of research models. In Dohrenwend, B., and Dohrenwend, B. (Eds.), *Stressful life events and their context* (pp. 202–222). Prodist, NY.

Graves, P. L., Want, N.-Y., Mead, L. A., Johnson, J. V., and Klag, M. J. (1998). Youthful precursors of midlife social support. *J. Personal. Soc. Psychol.* 74: 1329–1336.

Greenspan, F. S., and Baxter, J. D. (1994). *Basic and clinical endocrinology*. Appleton and Lange, Norwalk, Conn.

Gump, B. B., Polk, D. E., Kamarck, T. W., and Shiffman, S. M. (2001). Partner interactions are associated with reduced blood pressure in the natural environment: Ambulatory monitoring evidence from a healthy, multiethnic adult sample. *Psychosom. Med.* 63: 423–433.

Grewen, K. M., Girdler, S. S., Amico, J., and Light, K. C. (2005). Effects of partner support on resting oxytocin, cortisol, norepinephrine, and blood pressure before and after warm partner contact. *Psychosom. Med.* 67: 531–538.

Hawkley, L. C., Bosch, J. A., Engeland, C. G., Marucha, P. T., and Cacioppo, J. T. (in press). Loneliness, dysphoria, stress and immunity: A role for cytokines. In Plotnikoff, N. P., Faith, R. E., and Murgo, A. J. (Eds.), *Cytokines: Stress and immunity* (2nd edn.). CRC Press, Bocan Raton, LA.

Heinrichs, M., Baumgartner, T., Kirschbaum, C., and Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biol. Psychiatry.* 54: 1389–1398.

Hibbard, J. H., and Pope, C. R. (1993). The quality of social roles as predictors of morbidity and mortality. *Soc. Sci. Med.* 36: 217–225.

Holahan, C. J., and Moos, R. H. (1990). Life stressors, resistance factors, and improved psychological functioning: An extension of the stress resistance paradigm. *J. Personal. Soc. Psychol.* 58: 909–917.

Horsten, M., Mittleman, M. A., Wamala, S. P., Schenck-Gustafsson, K., and Orth-Gomer, K. (1999). Social relations and the metabolic syndrome in middle-aged Swedish women. *J. Cardiovasc. Risk.* 6: 391–397.

House, J. S. (2001). Social isolation kills, but how and why? *Psychosom. Med.* 63: 273–274.

House, J. S., Landis, K. R., and Umberson, D. (1988). Social relationships and health. *Science.* 241: 540–545.

Kamarck, T. W., Manuck, S. B., and Jennings, J. R. (1990). Social support reduces cardiovascular reactivity to psychological challenge: A laboratory model. *Psychosom. Med.* 52: 42–58.

Kaplan, G. A., Wilson, T. W., Cohen, R. D., Kauhanen, J., Wu, M., and Salonen, J. T. (1994). Social functioning and overall mortality: Prospective evidence from the Kuopio ischemic heart disease risk factor study. *Epidemiology.* 5: 495–500.

Kaplan, G. A., Salonen, J. T., Cohen, R. D., Brand, R. J., Syme, S. L., and Puska, P. (1988). Social connections and mortality from all causes and from cardiovascular disease: Prospective evidence from Eastern Finland. *Am. J. Epidemiol.* 128: 370–380.

Kiecolt-Glaser, J. K., McGuire, L., Robles, T. F., and Glaser, R. (2002). Emotions, morbidity, and mortality: New perspectives from psychoneuroimmunology. *Ann. Rev. Psychol.* 53: 83–107.

Kiecolt-Glaser, J. K., Loving, T. J., Stowell, J. R., Malarkey, W. B., Lemeshow, S., Dickinson, S. L., and Glaser, R. (2005). Hostile marital interactions, proinflammatory cytokine production, and wound healing. *Arch. Gen. Psychiatry*. 62: 1377–1384.

Knox, S. S., Adelman, A., Ellison, C. R., Arnett, D. K., Siegmund, K. D., Weidner, G., and Province, M. A. (2000). Hostility, social support, and carotid artery atherosclerosis in the National Heart, Lung, and Blood Institute Family Heart Study. *Am. J. Cardiol.* 86: 1086–1089.

Knox, S. S., and Uvnas-Moberg, K. (1998). Social isolation and cardiovascular disease: An atherosclerotic pathway? *Psychoneuroendocrinology* 23: 877–890.

Kop, W. J., Berman, D. S., Gransar, H., Wong, N. D., Miranda-Peats, R., White, M. D., Shin, M., Bruce, M., Krantz, D. S., and Rozanski, A. (2005). Social network and coronary artery calcification in asymptomatic individuals. *Psychosom. Med.* 67: 343–352.

Krause, N. (2001). Social support. In Binstock, R. H., and George, L. K. (Eds.), *Handbook of aging and the social sciences* (5th edn., pp. 272–294). Academic Press, NY.

Lee, M., and Rotheram-Borus, M. J. (2001). Challenges associated with increased survival among parents living with HIV. *Am. J. Public Health.* 91: 1303–1309.

Lepore, S. J. (1995). Cynicism, social support, and cardiovascular reactivity. *Health Psychol.* 14: 210–216.

Lepore, S. J. (1998). Problems and prospects for the social support-reactivity hypothesis. *Ann. Behav. Med.* 20: 257–269.

Levine, D. M., Green, L. W., Deeds, S. G., Chwalow, J., Russell, R. P., and Finlay, J. (1979). Health education for hypertensive patients. *J. Am. Med. Assoc.* 241: 1700–1703.

Levy, S. M., Herberman, R. B., Whiteside, T., Sanzo, K., Lee, J., and Kirkwood, J. (1990). Perceived social support and tumor estrogen/progesterone receptor status as predictors of natural killer cell activity in breast cancer patients. *Psychosom. Med.* 52: 73–85.

Lewis, M. A., and Rook, K. S. (1999). Social control in personal relationships: Impact on health behaviors and psychological distress. *Health Psychol.* 18: 63–71.

Libby, P. (2002). Inflammation in atherosclerosis. *Nature.* 420: 868–874.

Lin, N. (1986). Modeling the effects of social support. In Lin, N., Dean, A., and Ensel, W. (Eds.), *Social support, life events, and depression* (pp. 173–209). Academic Press, Orlando, Fla.

Linden, W., Chambers, L., Maurice, J., and Lenz, J. W. (1993). Sex differences in social support, self-deception, hostility, and ambulatory cardiovascular activity. *Health Psychol.* 12: 376–380.

Linden, W., Stossel, C., and Maurice, J. (1996). Psychosocial interventions for patients with coronary artery disease. *Arch. Intern. Med.* 156: 745–752.

Lutgendorf, S. K., Anderson, B., Sorosky, J. I., Buller, R. E., and Lubaroff, D. M. (2000). Interleukin-6 and use of social support in gynecologic cancer patients. *Int. J. Behav. Med.* 7: 127–142.

Lutgendorf, S. K., Sood, A. K., Anderson, B., McGinn, S., Maiseri, H., Dao, M., Sorosky, J. I., Geest, K. D., Ritchie, J., and Lubaroff, D. M. (2005). Social support, psychological distress, and natural killer cell activity in ovarian cancer. *J. Clin. Oncol.* 23: 7105–7113.

McCubbin, J. A., Kaplan, J. R., Manuck, S. B., and Adams, M. R. (1993). Opioidergic inhibition of circulatory and endocrine stress responses in cynomolgus monkeys: A preliminary study. *Psychosom. Med.* 55: 23–28.

Milagros, R. C., King, J., Ma, Y., and Reed, G. W. (2004). Stress, social support, and cortisol: Inverse associations? *Behav. Med.* 30: 11–21.

Miller, G. E., Cohen, S., and Ritchey, A. K. (2002). Chronic psychological stress and the regulation of pro-inflammatory cytokines: A glucocorticoid-resistance model. *Health Psychol.* 21: 531–541.

Miyazaki, T., Ishikawa, T., Nakata, A., Sakurai, T., Miki, A., Kawakami, N., Fujita, O., Kobayashi, F., Haratani, T., Iimori, H., Sakami, S., Fujioka, Y., Kawamura, N. (2005). Association between perceived social support and Th1 dominance. *Biol. Psychol.* 70: 30–37.

Moynihan, J. A., Larson, M. R., Treanor, J., Duberstein, P. R., Power, A., Shore, B., and Ader, R. (2004). Psychosocial factors and the response to influenza vaccination in older adults. *Psychosom. Med.* 66: 950–953.

Munck, A., Guyre, P. M., and Holbrook, N. J. (1984). Physiological functions of glucocorticoids in stress and their relation to pharmacological actions. *Endocr. Rev.* 5: 25–44.

Newsom, J. T., Nishishiba, M., Morgan, D. L., and Rook, K. S. (2003). The relative importance of three domains of positive and negative social exchanges: A longitudinal model with comparable measures. *Psychol. Aging.* 18: 746–754.

Ng, D. M., and Jeffery, R. W. (2003). Relationships between perceived stress and health behaviors in a sample of working adults. *Health Psychol.* 22: 638–642.

Ong, A. D., and Allaire, J. C. (2005). Cardiovascular intraindividual variability in later life: The influence of social connectedness and positive emotions. *Psychol. Aging.* 20: 476–485.

Olga, E., and Steptoe, A. (2001). Social support at work, heart rate, and cortisol: A self-monitoring study. *J. Occup. Health Psychol.* 6: 361–370.

Orth-Gomér, K., Rosengren, A., and Wilhelmsen, L. (1993). Lack of social support and incidence of coronary heart disease in middle-aged Swedish men. *Psychosom. Med.* 55: 37–43.

Patterson, T. L., Shaw, W. S., Semple, S. J., Cherner, M., McCutchan, J. A., Atkinson, J. H., Grant, I., and Nannis, E. (1996). Relationship of psychosocial factors to HIV progression. *Ann. Behav. Med.* 18: 30–39.

Perloff, D., Sokolow, M., and Cowan, R. (1983). The prognostic value of ambulatory blood pressure. *J. Am. Med. Assoc.* 249: 2793–2798.

Persson, L., Gullberg, B., Hanson, B. S., Moestrup, T., and Ostergren, P. O. (1994). HIV infection: Social network, social support, and CD4 lymphocyte values in infected homosexual men in Malmo, Sweden. *J. Epidemiol. Community Health*. 48: 580–585.

Perry, S., Fishman, B., Jacobsberg, L., and Frances, A. (1992). Relationships over 1 year between lymphocyte subsets and psychosocial variables among adults with infection by human immunodeficiency virus. *Arch. Gen. Psychiatry*. 49: 396–401.

Pierce, G. R., Lakey, B., Sarason, I. G., Sarason, B. R., and Joseph, H. J. (1997). Personality and social support processes: A conceptual overiew. In Pierce, G. R., Lakey, B., Sarason, I. G., and Sarason, B. R. (Eds.), *Sourcebook of social support and personality* (pp. 3–18). Plenum Press, New York.

Pressman, S. D., Cohen, S., Miller, G. E., Barkin, A., Rabin, B. S., and Treanor, J. J. (2005). Loneliness, social network size, and immune response to influenza vaccination in college freshmen. *Health Psychol.* 24: 297–306.

Rejeski, W. J., Thompson, A., Brubaker, P. H., and Miller, H. S. (1992). Acute exercise: Buffering psychosocial stress responses in women. *Health Psychol.* 11: 355–362.

Ross, R. (1999). Mechanisms of disease: Atherosclerosis—An inflammatory disease. *N. Engl. J. Med.* 340: 115–126.

Rowe, J. W., and Kahn, R. L. (1987). Human Aging: Usual and Successful. *Science*. 237: 143–149.

Rozanski, A., Blumenthal, J. A., and Kaplan, J. (1999). Impact of psychological factors on the pathogenesis of cardiovascular disease and implications for therapy. *Circulation* 99: 2192–2217.

Rozanski, A., Bairey, N., Krantz, D. S., Friedman, J., Resser, K. J., Morell, M., Hilton-Chalfen, S., Herstrin, L., Bietendorf, J., and Berman, D. S. (1988). Mental stress and the induction of silent myocardial ischemia in patients with coronary artery disease. *N. Engl. J. Med.* 318: 1005–1012.

Rutledge, T., Reis, S. E., Olson, M., Owens, J., Kelsey, S. F., Pepine, C. J., Mankad, S., Rogers, W. J., Merz, C. N. B., Sopko, G., Cornell, C. E., Sharaf, B., and Matthews, K. A. (2004). Social networks are associated with lower mortality rates among women with suspected coronary disease: The National Heart, Lung, and Blood Institute-sponsored Women's Ischemia Syndrome Evaluation study. *Psychosom. Med.* 66: 882–888.

Sarason, I. G., Sarason, B. R., and Shearin, E. N. (1986). Social support as an individual difference variable: Its stability, origins, and relational aspects. *J. Pers. Soc. Psychol.* 50: 845–855.

Schneiderman, N., Saab, P. G., Cateliier, D. J., Powell, L. H., DeBusk, R. F., Williams, R. B., Carney, R. M., Raczynski, J. M., Cowan, M. J., Berkman, L. F., and Kaufmann, P. G. for the ENRICHD Investigators (2004). Psychosocial treatment within sex by ethnicity subgroups in the Enhancing Recovery in Coronary Heart Disease clinical trial. *Psychosom. Med.* 66: 475–483.

Seeman, T. E. (1996). Social ties and health: The benefits of social integration. *Ann. Epidemiol.* 6: 442–451.

Seeman, T. E., Berkman, L. F., Blazer, D., and Rowe, J. W. (1994). Social ties and support and neuroendocrine function: The MacArthur studies of successful aging. *Ann. Behav. Med.* 16: 95–106.

Seeman, T. E., and Syme, L. (1987). Social networks and coronary artery disease: A comparison of the structure and function of social relations as predictors of disease. *Psychosom. Med.* 49: 341–354.

Smith, T. W., and Gallo, L. C. (2001). Personality traits as risk factors for physical illness. In Baum, A., Revenson, T., and Singer, J. (Eds.), *Handbook of health psychology* (pp 139–172). Lawrence Erlbaum, Hillsdale, NJ.

Spitzer, S. B., Llabre, M. M., Ironson, G. H., Gellman, M. D., and Schneiderman, N. (1992). The influence of social situations on ambulatory blood pressure. *Psychsom. Med.* 54: 79–86.

Steptoe, A., Lundwall, K., and Cropley, M. (2000). Gender, family structure and cardiovascular activity during the working day and evening. *Soc. Sci. Med.* 50: 531–539.

Taylor, S. E., Sherman, D. K., and Kim, H. S. (2005). Culture and social support: Who seeks it and why? *J. Pers. Soc. Psychol.* 87: 354–562.

Taylor, S. E., Klein, L. C., Lewis, B. P., Gruenewald, T. L., Gurung, R. A. R., and Updegraff, J. A. (2000). Biobehavioral responses to stress in females: Tend-and-befriend, not fight-or-flight. *Psychol. Rev.* 107: 411–429.

The ENRICHD Investigators. (2003). Effects of treating depression and low perceived social support on clinical events after myocardial infarction: The enhancing recovery in coronary heart disease patients (ENRICHD) randomized trial. *JAMA* 289: 3106–3116.

Theorell, T., Blomkvist, V., Jonsson, H., Schulman, S., Berntorp, E., and Stigendal, L. (1995). Social support and the development of immune function in human immunodeficiency virus infection. *Psychosom. Med.* 57: 32–36.

Thoits, P. A. (1995). Stress, coping, and social support processes: Where are we? What next? *J. Health Soc. Behav.* [extra issue], 53–79.

Thorsteinsson, E. B., and James, J. E. (1999). A meta-analysis of the effects of experimental manipulations of social support during laboratory stress. *Psychol. Health.* 14: 869–886.

Thorsteinsson, E. B., James, J. E., and Gregg, M. E. (1998). Effects of video-relayed social support on hemodynamic reactivity and salivary cortisol during laboratory-based behavioral challenge. *Health Psychol.* 17: 436–444.

Treiber, F. A., Kamarck, T., Schneiderman, N., Sheffield, D., Kapuku, G., and Taylor, T. (2003). Cardiovascular reactivity and development of preclinical and clinical disease states. *Psychosom. Med.* 65: 46–62.

Turner-Cobb, J. M., Sephton, S. E., Koopman, C., Blake-Mortimer, J., and Spiegel, D. (2000). Social support and salivary cortisol in women with metastatic breast cancer. *Psychosom. Med.* 62: 337–345.

Uchino, B. N. (2004). *Social support and physical health: Understanding the health consequences of relationships*. Yale University Press, New Haven, CT.

Uchino, B. N., Cacioppo, J. T., and Kiecolt-Glaser, J. K. (1996). The relationship between social support and physiological processes: A review with emphasis on underlying mechanisms and implications for health. *Psychol. Bull.* 119: 488–531.

Uchino, B. N., Cacioppo, J. T., Malarkey, W., Glaser, R., and Kiecolt-Glaser, J. K. (1995). Appraisal support predicts age-related differences in cardiovascular function in women. *Health Psychol.* 14: 556–562.

Uchino, B. N., Holt-Lunstad, J., Uno, D., and Betancourt, R. (1999). Social support and age-related differences in cardiovascular function: An examination of potential mediators. *Ann. Behav. Med.* 21: 135–142.

Uchino, B. N., Holt-Lunstad, J., Uno, D., and Flinders, J. B. (2001). Heterogeneity in the Social Networks of Young and Older Adults: Prediction of Mental Health and Cardiovascular Reactivity during Acute Stress. *J. Behav. Med.* 24: 361–382.

Umberson, D. (1987). Family status and health behaviors: Social control as a dimension of social integration. *J. Health Soc. Behav.* 28: 306–319.

Uvnas-Moberg, K. (1998). Oxytocin may mediate the benefits of positive social interaction and emotions. *Psychoneuroendocrinology* 23: 819–835.

Verma, S., Szmitko, P. E., and Yeh, E. T. H. (2004). C-reactive protein: Structure affects function. *Circulation*. 109: 1914–1917.

Wang, H.-X., Mittleman, M. A., and Orth-Gomer, K. (2005). Influence of social support on progression of coronary artery disease in women. *Soc. Sci. Med.* 60: 599–607.

Webster, J. C., Oakley, R. H., Jewell, C. M., and Cidlowski, J. A. (2001). Proinflammatory cytokines regulate human glucocorticoid receptor gene expression and lead to the accumulation of the dominant negative B isoform: A mechanism for the generation of glucocorticoid resistance. *PNAS*. 98: 6865–6870.

Welin, L., Larsson, B., Svärdsudd, T. B., and Tibblin, G. (1992). Social network and activities in relation to mortality from cardiovascular diseases, cancer and other causes: A 12 year follow up of the study of men born in 1913 and 1923. *J. Epidemiol. Community Health*. 46: 127–132.

Williams, R. B., Barefoot, J. C., Califf, R. M., Haney, T. L., Saunders, W. B., Pryor, D. B., Hlatky, M. A., Siegler, I. C., and Mark, D. B. (1992). Prognostic importance of social and economic resources among medically treated patients with angiographically documented coronary artery disease. *J. Am. Med. Assoc.* 267: 520–524.

Wills, T. A., and Yaeger, A. M. (2003). Family factors and adolescent substance use: Model and mechanisms. *Curr. Dir. Psychol. Sci.* 12: 222–226.