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Is Caregiving Hazardous to One's Physical Health? A Meta-Analysis

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Caring for a family member with dementia is generally regarded as a chronically stressful process, with potentially negative physical health consequences. However, no quantitative analysis has been conducted on this literature. The authors combined the results of 23 studies to compare the physical health of caregivers with demographically similar noncaregivers. When examined across 11 health categories, caregivers exhibited a slightly greater risk for health problems than did noncaregivers. However, sex and the health category assessed moderated this relationship. Stronger relationships occurred with stress hormones, antibodies, and global reported health. The authors argue that a theoretical model is needed that relates caregiver stressors to illness and proffers moderating roles for vulnerabilities and resources and mediating roles for psychosocial distress and health behaviors.

For the past 30 years researchers have assumed without controversy that providing care for an ill family member is hazardous to one's health. Although this research has been well meaning, no quantitative procedures have summarized this literature to assess the consistency of findings across studies. The fact is, it is still unknown to what extent caregiving is hazardous to one's health. In this meta-analysis we examine and critique the literature on self-reported health and physiological functioning in caregivers of persons with dementia. Because meta-analyses are usually restricted to studies with comparison groups (Shadish, Matt, Navarro, & Phillips, 2000), we focus here on research that compares caregivers with demographically similar noncaregivers. To provide a rationale for this review, we first discuss why caregiver health is important. We then argue that stressors, psychosocial distress, and risky health habits influence physiological responses in caregivers, which increase their risks for health problems. Next, we discuss how illnesses and physiological functioning have been measured in caregivers, as well as the rationales for the choice of measures. We then argue that inferences about relationships of caregiving with health problems should consider the types of health measures used. Finally, we note that research on caregiver health has been largely atheoretical and has not profited from extensive mind–body research. We conclude by recommending a model that uses constructs previously shown to be predictive of illnesses in persons under chronic stress.

Who Are Informal Caregivers and Why Are They Important?

Informal caregivers are caregivers who are not financially compensated for their services. They are usually relatives or friends who provide assistance to persons who are having difficulties with daily activities because of physical, cognitive, or emotional impairments. Without such help, care recipients, such as persons with Alzheimer's disease (AD), would not be able to sustain themselves. Although caregiving is dependent on the specific needs of each person, it usually involves helping with maintenance such as bathing or higher level activities such as reading. In general, caregiving is

> based on a reverence for life and the belief that human beings have the innate right to function to their highest level of mental and physical capacity. The major mission of caregiving is to promote independence by maintaining the person's most functional state—physically, intellectually, emotionally, and spiritually. (Bridges, 1995, p. 13)

Since prehistoric times, informal caregiving has been the standard way to protect people in poor health (Lebel et al., 2001). Although caregivers have always been of socioeconomic value to society, in the future they will be even more important. In the next 20 years, the portion of the U.S. population that will exceed 65 years of age will increase from 12% to 17% (U.S. Bureau of the Census, 1996). The prevalence of AD will also increase. Estimates of AD in the United States vary from 2.7% to 11.2% for persons 65 years of age or older (Ernst & Hay, 1997). This translates to 1.5–6.1 million persons. Note that although 75% of all persons with dementia who are 65 years of age or older have AD (Ganguli, Dodge, Chen, Belle, & DeKosky, 2000), stroke and Parkinson's

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disease also create cognitive and behavioral problems (Hooker, Manoogian-O'Dell, Monahan, Frazier, & Shifren, 2000; Vetter et al., 1999). Thus, the prevalence of all dementias, and the resulting costs, are significantly greater than those for AD alone. For 1991 the total U.S. costs of AD alone were $20 billion (Johnson, Davis, & Bosanquet, 2000), and families bore most of these expenses (Leon, Cheng, & Neumann, 1988). Unfortunately, the costs of caregiving may also be psychosocial and physical.

Why Are Caregivers Expected To Be at Higher Risk for Health Problems Than Noncaregivers?

Given the critical functions that caregivers perform, both government agencies and researchers have been concerned with maintaining caregiver health. One assumption underlying this concern is that negative responses to caregiving may interfere with a caregiver's ability to provide care. However, researchers have also been concerned with caregiver health in its own right—and concerned that caregivers may not care for or be able to care for themselves. These beliefs have generated extensive research. Since Grad and Sainsbury (1963), the first researchers to examine perceptions of stressors among caregivers, a plethora of observational studies have been performed. Most of these studies did not include comparison groups. In those that did, matching was not always used to control confounders. In studies that matched on variables, such as sex and age, the direction of relationships between caregiving and health indicators could not be determined because of the retrospective designs. Despite these problems, researchers have persisted in studying caregiver health because of its importance to society and the assumption that caregivers are at risk for illnesses. We now discuss two literatures to support the belief that caregivers are at risk for health problems. First we consider caregiver experiences, such as chronic stressors, psychosocial distress, and risky health habits, and then we review relationships known to exist among chronic stress, distress, health habits, health indicators, and potential physiological mechanisms.

Stressors, Distress, and Health Habits in Caregivers

To understand the stressors encountered by caregivers of victims of dementia and related disorders, one needs to understand these diseases. Dementia is caused by degenerative brain (AD), cerebrovascular (multi-infarct dementia), and neurological (Parkinson's) diseases. AD and vascular dementia are diagnosed using established criteria (*Diagnostic and Statistical Manual of Mental Disorders*, 4th ed.; *DSM–IV*; American Psychiatric Association, 1994; McKhann et al., 1984). AD involves impairments in memory, attention and cognition, and gradual progressive intellectual and functional deterioration. Parkinson's disease involves progressive degeneration of motor function, tremors, and stiffness (Stern, 1988). Most caregivers of persons with dementia face 3–15 years of exposure to physical and psychosocial demands. They absorb household chores and are exposed to symptoms of depression, anger, agitation, and paranoia in their care recipients (Teri et al, 1992). These affects and behaviors intrude on their lives (Mendelsohn, Dakof, & Skaff, 1995; Vernon & Stern, 1988). As AD progresses, caregivers must continually monitor their care recipients and witness their cognitive deterioration (Stephens, Kinney, & Ogrocki, 1991). This exposure to chronic stressors can lead to psychosocial distress and risky health behaviors.

One psychosocial response to caregiving is perceived burden. It results from the "physical, psychological, emotional, social and financial problems experienced by families caring for impaired older adults" (George & Gwyther, 1986, p. 253). Burden includes embarrassment, overload, feelings of entrapment, resentment, isolation from society (Zarit, Reever, & Bach-Peterson, 1980), loss of control, poor communication, (Morris, Morris, & Britton, 1988), and work pressures (Stephens et al., 1991). Given these responses, it is not surprising that caregivers report more distress and risky health behaviors than do noncaregivers. As an example, Blazer (2003) reviewed three population-based studies of community-residing older adults and reported a median rate of major and minor depression of 11%. In contrast, in a review of caregiver morbidities, the median rate of clinical depression (e.g., using versions of the Structured Clinical Interview for *DSM–IV*) was 22% (Schulz, O'Brien, Bookwala, & Fleissner, 1995). When self-report measures were used, however, the median rate of depressed mood was 30%. These results are consistent with reviews that have argued that rates of clinical depression in caregivers are significantly higher than in the general population but that only a minority of caregivers will meet with clinical depression if they are not actively seeking psychological intervention (Neundorfer, 1991; Wright, Clipp, & George, 1993). These results also support the belief that structured interviews yield lower estimates of depression than self-report inventories. In addition to depression, other reactions may increase the risks of caregiver illnesses. These include sleep problems, poor diets, and sedentary behaviors (Fuller-Jonap & Haley, 1995; Gallant & Connell, 1997; Vitaliano et al., 2002).

Relationships of Chronic Stressors With Health Indicators

Chronic stressors are associated with illnesses (S. Cohen, Kessler, & Underwood-Gordon, 1997; Greenwood, Muir, Packham, & Madeley, 1996) and with disease progression in persons who are already ill (Everson et al., 1997). Caregivers may experience prolonged anticipatory bereavement over lost aspects of their relationships with their care recipients, and bereavement is positively associated with physical illnesses (Kaprio, Koskenvuo, & Rita, 1987), health care utilization (Prigerson et al., 1997; W. Stroebe & Stroebe, 1987), and mortality (Goldman, Korenman, & Weinstein, 1995). Chronic stressors and bereavement are also associated with elevated physiological risks (Kawakami, Haratani, & Araki, 1998; B. S. McCann et al., 1999; O'Connor, Allen, & Kaszniak, 2002; Pickering et al., 1996). Such responses may provide mechanisms for why chronic stressors are related to illness.

Two pathways may be relevant to relationships of illness with chronic stressors and bereavement. One pathway appears to flow from chronic stressors to psychosocial distress and then to stress hormones. This primarily occurs via the hypothalamic–pituitary–adrenal axis, from which corticotropin releasing hormone-ACTH-cortisol are secreted, and the sympathetic adrenomedullary axis, from which norepinephrine and epinephrine are secreted (Lovallo, 1997; Steptoe, Cropley, Griffith, & Kirschbaum, 2000). These hormones stimulate peripheral activity, which can lead to *allostatic load*, or wear-and-tear from repeated arousal and inefficient control of physiological responses (Chrousos & Gold, 1992; McEwen, 2000). Such compensation may lead to pathophysiology (Niaura, Stoney, & Herbert, 1992; Schneiderman, 1983). In a second path-

way, distress may trigger risky health behaviors, such as poor diet, sedentary behavior, and substance abuse.

These two possible pathways, among others, may contribute to illness by increasing cardiovascular (Kannel & Vokonas, 1986), metabolic (Keys, Fidanza, Karvonen, Kimura, & Taylor, 1972), or immunologic (O'Leary, 1990) dysregulation. As such, they should help to explain why depression, sleep problems, and risky behaviors are associated with illnesses in the general population (Arntzenius et al., 1985; Epstein & Perkins, 1988; Erikssen, Forfang, & Jervell, 1981; Fischer & Raschke, 1997; Leigh & Fries, 1992; Musselman, Evans, & Nemeroff, 1998) and why caregivers are expected to be at greater risk for illnesses.

Current Knowledge About Physical Health Indicators in Caregivers

In one review (Schulz, Visintainer, & Williamson, 1990), only 11 of 34 caregiver studies examined physical health, and only 1 study included physiological measures. In studies that used self-reports, the measures included global self-reported health, a single item that assessed health from "poor" to "excellent" (Davies & Ware, 1981); number and intensity of symptoms (Pennebaker, 1982); number of chronic illnesses (Rosencranz & Pihlblad, 1970); number of medications (Harrison, 1997); and health care utilization (Ritter et al., 2001). Caregivers were similar to matched noncaregivers in some studies (George & Gwyther, 1986), but poorer in health in other studies (Haley, Levine, Brown, Berry, & Hughes, 1987). In a review of 40 additional studies (Schulz et al., 1995), some researchers found that caregivers were higher than noncaregivers in chronic illnesses and medications (Baumgarten et al., 1992; Kiecolt-Glaser, Dura, Speicher, Trask, & Glaser, 1991), whereas others did not observe differences (George & Gwyther, 1986; Haley et al., 1987). Since these reviews, more studies have used physiological measures. Such measures may help to explain observed associations between caregiving and illness. Indeed, physiological measures may show associations with caregiver experiences much earlier than do chronic illnesses.

Physiological Indicators

Table 1 contains a list of the categories and measures that have been used to study physiological functioning in caregivers since this research began 15 years ago. The categories include stress hormones and neurotransmitters and, immunologic, cardiovascular, and metabolic functioning. For each measure, we provide its description and the references that support its relationships with stress and illness. We do not consider the caregiver studies that have examined these measures because they are discussed below. We now argue that the type of health measure used may influence its relationship with caregiving.

Health Indicators as Moderators

Because caregiver health problems have been assessed in many different ways, it is important to examine whether certain measures are more related to caregiving than others. If some health problems are more associated with caregiving than others, this could have both theoretical and clinical implications. Hence, one objective of this article was to consider four contrasts, each of which is driven by previous work. First, self-report measures may have inherent advantages over physiological measures because of their relationships with distress. That is, strong positive relationships exist between caregiving and psychological distress (Schulz et al., 1995) and between distress and reported health problems (Costa & McCrae, 1980; Watson & Clark, 1984). Thus, one needs to assess whether caregiving is more related to reported health than to physiological measures. Second, because relationships are especially high for global self-reported health with distress ($r = .70$; Hooker & Siegler, 1992), it would be useful to assess whether relationships of caregiving with global health are greater than relationships of caregiving with reports of medications, utilization, and illnesses. Third, researchers in psychophysiology would expect measures that are immediately responsive to central nervous system arousal, such as stress hormone levels, to be more related to caregiving than more peripheral cardiovascular and metabolic responses (Lovallo & Thomas, 2000). Fourth, variations in the association of caregiving with immunity are relevant to research in psychoneuroimmunology. For example, meta-analyses of immune measures with depression and stress have reported that mean effect sizes for antibodies to viruses are larger than mean effect sizes for T-cell counts and natural killer cell activity (NKA; Herbert & Cohen, 1993a, 1993b). In addition to health indicators, individual differences may be moderators of relationships of caregiving with health problems. However, prior to presenting some candidates, we consider a model that supports the importance of individual differences for predicting health problems in caregivers.

A Theoretical Model of Caregiver Experiences, Individual Differences, and Health Problems

Although research on caregiver health has steadily increased in the past decade, relatively few attempts have been made to use a theoretical model to unify this work. Figure 1 is one such attempt. It illustrates the basic pathways that interrelate caregiver stressors, psychosocial distress, risky health habits, physiological mediators, and subsequent health problems. The model overlaps and parallels previous attempts to relate psychosocial factors to illness (Clark, Anderson, Clark, & Williams, 1999; Jorgensen, Johnson, Kolodziej, & Schreer, 1996; Taylor & Repetti, 1997). It includes individual differences, such as vulnerabilities and resources, that moderate relationships of stressors with distress (Lazarus & Folkman, 1984). Vulnerabilities and resources tend to be negatively related. As such, some researchers have viewed them as mirror images or opposite ends of the same continuum. However, there is some tradition in sociology, psychology, epidemiology, and psychiatry to distinguish these constructs according to their stability and temporal place among pathways from stressors to illness. For example, the term *vulnerability* has been used to refer to hard-wired characteristics (Mechanic, 1967) such as age, sex, disposition (Lazarus & Folkman, 1984), race (Robins, 1978), and family history and heredity (Zubin & Spring, 1977). In contrast, resources are more mutable and affected by interactions of the person with the environment. These include process coping (Folkman & Lazarus, 1980) and social supports (S. Cohen & Wills, 1985). For these reasons, vulnerabilities typically occur early in development and are not the result of caregiving, whereas resources may be both predictors and outcomes of caregiving. Using this framework, traitlike characteristics, such as dispositions, may have positive (e.g., hostility) or negative (e.g., optimism) relationships with illness, depending on their content, but

they are both categorized in the vulnerability domain. Hence, persons high in optimism would be low in vulnerability. Likewise, depending on their quality, social supports may provide either high or low resources.

Given the model, one would expect the main effects of exposures (*E*; here, caregiving), vulnerabilities (*V*), and resources (*R*) to be directly associated with psychosocial distress and risky health habits. In addition, interactions among the constructs' indicators are expected to influence illness over and above the main effects. This belief is consistent with the stress–diathesis model (Mechanic, 1967). For example, two-way interactions of exposures, vulnerabilities, and resources (e.g., $E \times V$; E/R; V/R) predict distress and poorer health habits beyond the main effects of *E*, *V*, and $1/R$, and they also magnify their effects (Vitaliano, Maiuro, Bolton, & Armsden, 1987). Indeed, in one study caregivers with high vulnerability and low resources (V/R) had greater burden 15–18 months later than did those with either low vulnerability or high vulnerability and high resources, even after controlling baseline burden (Vitaliano, Russo, Young, Teri, & Maiuro, 1991). One would expect such distress to result in greater illness risks for these caregivers.

Individual Differences as Moderators

Consistent with Figure 1, another objective of this article was to assess whether relationships of caregiving with health problems are moderated by individual differences. Examples of some candidates for moderation include psychiatric history, personality, ethnicity, comorbidities, social supports, socioeconomic status (SES), and coping. In support of the stress–diathesis model, Russo, Vitaliano, Brewer, Katon, and Becker (1995) found that 73% of caregivers with a history of depression had a recurrence of depression while they were caregivers, but only 30% of noncaregivers had a recurrence during a similar time frame. This is important because depression has been found to be positively related to health problems in caregivers (Schulz et al., 1995). Caregivers also have elevated levels of anger (Gallagher, Wrabetz, Lovett, Del Maestro, & Rose, 1989), and Vitaliano, Becker, Russo, Magana-Amato, and Maiuro (1989) found that caregivers who were critical of their spouses in a structured interview reported more trait anger than those who were not critical of their spouses. These results are relevant to caregiver health because in noncaregivers, anger is a risk factor for elevated blood pressure (Jamner, Shapiro, Goldstein, & Hug, 1991), greater body mass index (Scherwitz, Perkins, Chesney, & Hughes, 1991), fat and caloric intake (Scherwitz et al., 1991), and glucose and insulin levels (Raikkonen, Keltikangas, & Hautanen, 1994). Indeed, caregivers high in anger have higher levels of fasting glucose than do noncaregivers who are high in anger, but no differences exist in caregivers and noncaregivers who are low in anger (Vitaliano, Scanlan, Krenz, & Fujimoto, 1996). Ethnicity may also be relevant to caregiver health because it is related to health disparities (Kaplan, 1992), and ethnic groups respond differently to caregiving (Hinrichsen & Ramirez, 1992). Also, Black caregivers may have fewer economic resources than White caregivers, but they may have more spiritual resources (Dilworth-Anderson & Anderson, 1994). Finally, comorbidities, such as coronary heart disease (CHD) and cancer may moderate relationships between caregiving and physiological measures that are manifestations of these diseases (Vitaliano, Scanlan, Ochs, et al., 1998; Vitaliano, Scanlan, Siegler, et al., 1998).

In noncaregivers, resources such as emotional and instrumental supports (House, 1981) are related to better health habits (Peirce, Frone, Russell, Cooper, & Mudar, 2000), less distress (Raikkonen et al., 1994), and lower CHD prevalence (Niaura et al., 1992; Williams et al., 1992). In caregivers, high levels of perceived support also predict better reported health (Monahan & Hooker, 1995) and lower metabolic and cardiovascular risk (Vitaliano et al., 2002). In noncaregivers, high SES is associated with better physical health (Adler & Ostrove, 1999) and lower CHD prevalence (Niaura et al., 1992), and low SES is related to poorer health in caregivers (Morrissey, Becker, & Rupert, 1990). Active coping, such as problem solving, is inversely associated with elevated distress (Folkman & Lazarus, 1980), poor health habits (Epstein & Perkins, 1988), and physiological risk (Niaura et al., 1992) in noncaregivers. In caregivers, problem-focused coping is associated with less psychological distress (Vitaliano, Russo, Carr, Maiuro, & Becker, 1985).

Demographic variables, such as a caregiver's age, relationship to the care recipient, and sex may be particularly relevant to his or her risk of illness. In two of three studies reviewed by Schulz et al. (1995), women reported greater health problems than did men, and in two of two studies of caregiver age, no relationships were observed with health (Schulz et al., 1995). However, these were relationships for health problems with individual differences and not relationships of effect sizes with individual differences. To our knowledge, no studies have examined the latter. It is important to note that the direction of moderation was, and still is, not obvious for sex, age, and one's relationship to the care recipient. Although older persons have less resistance to illness (Rowe & Kahn, 1998), caregiving may be more developmentally on time for older than for younger caregivers (Neugarten, 1969). Also, spouses may be frailer, more isolated, and more distressed than other caregivers (C. A. Cohen et al., 1993), but caring for a spouse might be viewed as a marriage commitment. In contrast, caring for a parent might pose conflicts of equity when one must choose between parents versus spouses and children (George, 1982). Sex may be an important moderator of caregiver health because women report more distress (Kessler et al., 1994) and health problems (Rahman, Strauss, Gertler, Ashley, & Fox, 1994; Ross & Bird, 1994), and they utilize more health care (Nathanson, 1990) than do men. Alternatively, men exposed to laboratory stressors show larger and more consistent increases in stress hormones, neurotransmitter metabolites, and blood pressure than do women (Earle, Linden, & Weinberg, 1999; Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999). This may be further exacerbated when faced with a stressor such as caregiving, which is inconsistent with men's traditional gender roles (Kramer, 1997). Finally, widowers appear to have more illnesses in response to the loss of a spouse than do widows (Chen et al., 1999). Hence, one might expect associations of caregiving and health indicators to differ for men and women.

Study Objectives

Given the contributions that caregivers make to society and the potential for improving understanding of relationships of chronic stressors with illness, one goal of this article is to quantify relationships of caregiving with health problems. For practical and

Table 1
Measures of Stress and Physiological Functioning in Caregiver Research

Measure	Description	Stress related	Illness related
	Stress hormones and neurotransmitters		
ACTH	(Adrenocorticotropic hormone) Peptide hormone secreted by pituitary signal cortisol release.	Chrousos & Gold (1992), Lovallo (1997), Lovallo & Thomas (2000)	
Cortisol	Steroid glucocorticoid secreted by the adrenal gland. Affects cardiac and metabolic function.	Chrousos & Gold (1992), Lovallo (1997), Lovallo & Thomas (2000)	Chrousos & Gold (1992), Lovallo (1997), Lovallo & Thomas (2000), Sapolsky (2000)
Epinephrine	Secreted rapidly by adrenal medulla. Affects cardiac function and blood pressure (BP).	Lovallo (1997), Lovallo & Thomas (2000)	
Norepinephrine	Present in CNS, peripheral sympathetic nerves, and the adrenal medulla. Secretion affected by muscular exertion and effort. Affects cardiac function, BP, and immunity.	Lovallo (1997), Lovallo & Thomas (2000)	Kohm & Sanders (2001)
Prolactin	Peptide hormone secreted by anterior pituitary. Can increase with high physical and/or psychological stress exposure. Has an immune stimulating effect.	Irwin et al. (1997)	McMurray (2001)
Forskolin stimulation	Stimulates post-beta receptor adenylate cyclase activation. May be used to test changes in cyclic AMPA independent of beta-2 receptors.	Mills et al. (1997)	
Growth hormone	Growth hormone mRNA expression from B and T cells facilitates immunity. Low levels of growth hormone mRNA expression suggest reduced growth hormone production.	Wu et al. (1999)	Lovallo (1997), Lovallo & Thomas (2000), McCallum et al. (2002)
GABA	The neurotransmitter GABA is known to counter certain stress responses in animals. Neurotransmitters found in cerebrospinal fluids (CSF) reflect CNS activity. Low CSF GABA has been found in people with depression.	Pomara et al. (1989), Sanacora et al. (2000)	
Neuropeptide Y	Neurotransmitter in both CNS and peripheral sympathetic nerves, which increases catecholamine activities and influences feeding behaviors.	Irwin et al. (1991), Zukowska-Grojec (1995)	Irwin et al. (1991), Zukowska-Grojec (1995)
Beta receptors	Beta-adrenergic receptors mediate relationships among catecholamines, cardiac function, and BP.	Naga-Prasad et al. (2001)	Haeusler (1990), Herd (1991), Naga-Prasad et al. (2001)
	Immunologic		
Cellular			
Enumerative	Cell counts, percentages, and CD4:CD8 ratios. High levels of some immune cells are generally associated with health, others with infectious illness; for example, high white blood cell count is generally associated with active infections; CD3 refers to total T lymphocyte cell count; CD4 cells are generally considered to be positively related to the capacity to defend against many illnesses. Low CD4 can be caused by severe disease, such as HIV infection, and reflects disease vulnerability. High CD8 (cytotoxic T cells) counts may reflect an overactive immune system or a current illness the immune system has difficulty controlling. CD4:CD8 ratio is used as an immunological index, with higher ratios presumed healthier. Higher NK (CD56) and B-cell counts are generally thought to reflect better immune reserves.	Cohen & Herbert (1996), Herbert & Cohen (1993a, 1993b), Lovallo (1997), Lovallo & Thomas (2000)	Cohen & Herbert (1996), Herbert & Cohen (1993a, 1993b), Lovallo (1997), Lovallo & Thomas (2000)
Functional	Lymphocyte proliferation in response to mitogen challenge. Index of the ability of T and B cells to proliferate in response to mitogens such as phytohemagglutinin, concanvillan A, and poke weed. Low levels may suggest illness susceptibility.	Cohen & Herbert (1996), Herbert & Cohen (1993a, 1993b), Irwin (1999), Lovallo (1997), Lovallo & Thomas (2000)	Horiuchi et al. (1995), Irwin (1999)
	Natural killer cell activity (NKA) and lymphokine activated killing are early immunological defenses against tumor cells and viral infections independent of prior exposure. Common measures of NKA include unstimulated killing response to tumor cells and response to tumor cells after cytokine stimulation (such as IL-2 or interferon gamma), which may better reflect in vivo NKA. Moderate to high NKA is consistent with good health; chronically low NKA may reflect disease susceptibility.	Cohen & Herbert (1996), Herbert & Cohen (1993a, 1993b), Lovallo (1997), Lovallo & Thomas (2000)	Lovallo (1997), Lovallo & Thomas (2000)

Table 1 (*continued*)

Measure	Description	Stress related	Illness related
	Immunologic (*continued*)		
Cellular Functional (*continued*)	Delayed type hypersensitivity response is skin's capacity to respond to multiple antigens (J. J. McCann, 1991, used tuberculin, tetanus, streptococcus, diptheria, candida, trichophyton, and proteus), usually 48 hr after exposure. Two typical response measures are the number of positive antigen reactions (antigen score) and the size (diameter) of the antigenic skin response (induration).	Dhabhar (2000)	Dannenberg (1991)
	Healing speed of a standardized skin puncture wound is used as a general health index, and is dependent on interactions of immunological, hormonal, and nutritional factors.	Kiecolt-Glaser et al. (1995)	Kiecolt-Glaser et al. (1995)
	Tumor necrosis factor is an inflammatory cytokine. High levels are thought to promote loss of muscle tissue, aging, and poor general health. Cytokine secretion has complex effects on immunological responses and can affect cellular immune responses (such as activating macrophages) and humoral immunity through beta-cell activation.	Dantzer et al. (1999), Lovallo (1997), Lovallo & Thomas (2000)	Dantzer et al. (1999), Lovallo (1997), Lovallo & Thomas (2000)
	Antibodies		
Vaccinations	Immunoglobulin G (IgG) vaccination response (influenza and otherwise). High antibody responses reflect health. A four-fold + memory response postvaccination implies a vigorous immune response.	Cohen & Herbert (1996), Herbert & Cohen (1993a, 1993b), Lovallo (1997), Lovallo & Thomas (2000)	Cohen & Herbert (1996), Herbert & Cohen (1993a, 1993b), Lovallo (1997), Lovallo & Thomas (2000)
Epstein Barr virus (EBV)	EBV virus capsid antigen IgG titers. High levels of EBV antibodies, in the absence of vaccination or antigenic challenge, may reflect latent EBV viruses that the cellular immune system is having difficulty suppressing.	Cohen & Herbert (1996), Herbert & Cohen (1993a, 1993b), Lovallo (1997), Lovallo & Thomas (2000)	Murray & Young (2002)
Immunoglobulins	A GAM profile includes measures of multiple plasma immunoglobulins (IgG, IgA, IgM). Although different diseases can result in either increases or decreases in immunoglobulins, in the absence of specific disease, it is assumed that lower levels are associated with poorer immunity. These are relatively general measures as opposed to specific immunological memory responses, such as antibody responses to influenza vaccination.	Valdimarsdottir & Stone (1997)	Pyne & Gleeson (1998)
	Cardiovascular		
Systolic BP (SBP)	The point of highest recorded BP, usually measured at rest. SBP ≥ 140 suggests hypertension, which is associated with coronary heart disease (CHD) and mortality.	Herd (1991), Lovallo (1997), Lovallo & Thomas (2000)	Herd (1991), Lovallo (1997), Lovallo & Thomas (2000)
Diastolic BP (DBP)	The point of lowest recorded BP, usually measured at rest. DBP ≥ 90 suggests hypertension.	Herd (1991), Lovallo (1997), Lovallo & Thomas (2000)	Herd (1991), Lovallo (1997), Lovallo & Thomas (2000)
Heart rate	Measured in heart beat/min. Higher rates may be associated with reduced heart function.	Herd (1991), Lovallo (1997), Lovallo & Thomas (2000)	Herd (1991), Lovallo (1997), Lovallo & Thomas (2000)
	Metabolic		
Insulin, glucose obesity	Insulin anabolic hormone causes glucose storage; hyperinsulinemia reflects difficulty controlling glucose.	Schneiderman & Skyler (1996)	Schneiderman & Skyler (1996)
	Glucose is necessary for muscular activity and proper brain function, but high fasting glucose (126+) suggests glucose intolerance and possible diabetes, conditions associated with CHD.	Schneiderman & Skyler (1996)	Schneiderman & Skyler (1996)
	Body mass index is the ratio of weight/height squared. High numbers reflect obesity.	Schneiderman & Skyler (1996)	Schneiderman & Skyler (1996)
Transferin	Transferin is an index of stored iron in the body. Low iron levels may be associated with anemia.		Bostian et al. (1976)
Plasma lipids	Low-density cholesterol and triglycerides are associated with obesity and CHD. High-density cholesterol is associated with physical fitness and reduced CHD.	Schneiderman & Skyler (1996)	Schneiderman & Skyler (1996)

Note. CNS = central nervous system; AMPA = alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid; GABA = gamma-aminobutyric acid; CD = cluster designation; NK = natural killer; IL-2 = interleukin 2; GAM = profile for immunoglobulins G, A (IgA), and M (IgM).

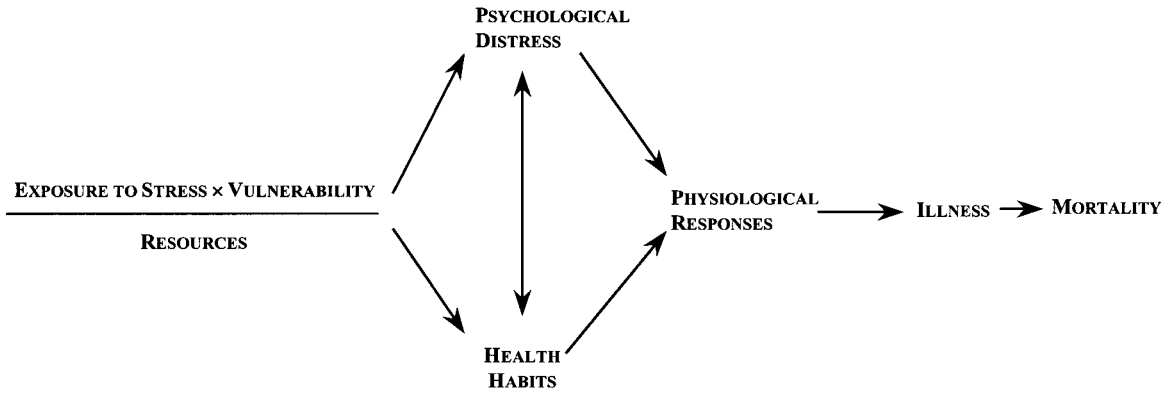

Figure 1. Theoretical model of stress and health/illness.

theoretical reasons, however, we also examine whether certain health indicators are more related to caregiving than others and whether some subgroups of caregivers are at greater risk for health problems. A final objective is to critique the state of research in this area and provide recommendations for future work.

Method

Inclusion and Exclusion Criteria Used to Search the Caregiver Physical Health Literature

We located reports using electronic and manual searches and the reference lists of identified articles. We sampled Current Contents since 1996, MEDLINE since 1983, PsycINFO since 1967, Sociofile since 1974, Social Work Abstracts since 1977, and Nursing and Allied Health since 1982. To be included, a report had to examine caregivers of persons with dementia and physical health problems or illnesses or physiology. In each database we included the following key words or word stems—using an asterisk as "wild card," here indicating that the search contained but was not limited to that word or word stem: *dementia*, *Alzheimer's disease*, *cognitive disorders*, *health*, *physical and health*, *physiolog**[1], *illness**, *hormones*, *cholesterol*, *cardiovascular diseases*, *blood pressure*, *obesity*, *diabetes*, *immun**, *mortality*, *death*, and *caregiv**[2]. Articles were searched only in English, with an inclusion end date of April 1, 2001. Medical subject headings (MeSH, the National Library of Medicine vocabulary) were also used for MEDLINE articles. We also hand searched the *Journals of Gerontology*, *The Gerontologist*, the *Journal of the American Geriatrics Society*, *Psychology and Aging*, *Psychosomatic Medicine*, *Health Psychology*, the *Journal of Behavioral Medicine*, the *Annals of Behavioral Medicine*, the *Journal of the American Medical Association*, and the *Journal of Aging and Health*. Bibliographies from reviews were also used (Schulz et al., 1990, 1995; Vitaliano, 1997). We excluded articles that (a) were non-data based, (b) examined caregivers of care recipients who did not have dementia (e.g., cancer patients), (c) did not include health or physiological data, and (d) lacked a noncaregiver comparison group. Because we could not guarantee that all studies were uncovered, we examined the robustness of our findings from all possible reports of data censoring. To do this, we used the "trim and fill" procedure (Sutton, Song, Gilbody, & Abrams, 2000), which is described below.

Results of searches. For parsimony we provide only the results for MEDLINE, as it yielded the vast majority of articles. After crossing the key words *dementia* (*Alzheimer's*) by *caregiv** by *physical health* (or *immunity*, *physiology*, *cardiovascular diseases*, *endocrinology*), we obtained 81 articles. When these terms were crossed by *control*, *noncaregiver*, or *comparison*, 35 articles resulted. The other databases yielded 7 additional articles. Hence, 42 (35 + 7) of 88 articles, or 48%, met criteria. Using similar key words in the ProQuest Digital Dissertations database (UMI from 1984), we obtained 10 entries; however, only 3 were retained (Atkinson, 1995; Giefer, 1994; J. J. McCann, 1991) because the others had been published and included above or they did not include physical health data or noncaregivers. This resulted in 45 reports.

Independence of samples. To clarify whether multiple reports from one research group came from independent samples, we compared the demographic data and descriptions of participants. Three labs produced reports with partial to substantial participant overlap. These authors were contacted, and it was determined that the Ohio State University (OSU) and University of California, San Diego (UCSD) labs used three and two independent samples, respectively, and the University of Washington (UW), University of Alabama, and Medical College of Georgia each used one sample. Of the three dissertations, two used independent samples, and the third was based on data from the second OSU sample that had not been published (Atkinson, 1995). Overall, the 42 articles and one dissertation were generated from 21 independent samples, and two dissertations were generated from 2 independent samples. This yielded a total of 23 samples. Eighteen samples each produced 1 report, and 5 samples produced 27 reports. Of the latter, 10 articles were from the OSU laboratory, 8 articles were from the UW laboratory, 5 articles were from the UCSD laboratory, and 2 articles each were from the University of Alabama and the Medical College of Georgia.

Health Categories Assessed

Table 2 summarizes the 45 reports according to the 23 samples that generated them. For each report there are eight main columns containing the (a) identifying number of the sample; (b) report's authors and year of publication; (c) mean ages of the caregivers and noncaregivers; (d) types of disorders of the care recipients; (e) caregiver sample size, stratified on sex; (f) noncaregiver (control) sample size, stratified on sex; (g) types of reported health measures; and (h) types of physiological measures. Eleven samples used only reported health measures, six used only physiological measures, and six used both. There were five self-reported health categories and six physiological categories.

Five reported health categories. Table 2 includes the report references for each category, so they are not repeated here.

1. Global self-reported health was examined in 10 samples (n = 717 caregivers; n = 879 noncaregivers). Five samples used a single self-rated item, "How would you rate your current health?" on a 4-point or 5-point scale from *poor* to *excellent*. As noted below, these scores were reversed in the analysis so that a

[1] This subsumes terms such as *physiology* and *physiological*.

[2] This subsumes terms such as *caregiver*, *caregivers*, and *caregiving*.

Table 2
Summary of the 45 Reports Included in the Meta-Analysis

Sample	Report	Mean age	Care recipients	CG		CO		Self-reported measures	Physiological measures
				M	W	M	W		
1	Kiecolt-Glaser et al. (1987)	CG: 59.3; CO: 60.3	AD	11	23	11	23	Global self-reported health, number of physician visits, number of days ill	NK cell percentage, CD#, CD4, CD4:CD8 ratios, EBV antibody; EBV VCA IgG titers, albumin, transferin
2	Cacioppo et al. (1998)	CG and CO: 67.2	AD or other dementia	0	27	0	37		Proliferation (ConA, PHA), NKA, NK cell count, CD3, CD4, CD8, CD4/CD8
	Esterling et al. (1994)	CG: 70.4; CO: 70.9	AD	10	21	9	22	Number of chronic conditions, number of physician visits, number of days ill	NKA, NK cell percentage, NKA response to rIFN or rIL-2, mean cell fluorescence
	Esterling et al. (1996)	CG: 65.7; CO: 68.9	AD or other dementia	10	18	7	22		NKA, NK cell's response to rIFN or rIL-2, BMI
	Glaser & Kiecolt-Glaser (1997)	CG: 60.6; CO: 62.4	AD, Parkinson's disease, Huntington Picks disease	13	58	13	45	Percentage with cold sore history	Herpes antibody titers, HSV-1 specific T-cell response
	Kiecolt-Glaser et al. (1991)	CG: 67.3; CO: 67.8	AD, multi-infarct dementia, Parkinson's disease, Huntington Picks disease, unspecified dementia	20	49	20	49	Number of chronic conditions, number of physician visits, number of days ill	ConA, PHA, NK cell percentage, CD3, CD4, CD8, B cell, EBV VCA IgG titers
	Kiecolt-Glaser et al. (1996)	CG: 73.1; CO: 73.3	AD	14	18	14	18		CD3, CD4, CD8, monocytes, IgG response to vaccination (ELISA), IgG response to vaccination (HAI), cytokine response: IL-1b, cytokine response: IL-6, cytokine response: IL-2
	Uchino et al. (1992)	CG and CO: 63.5 (*Mdn*)	AD	13	23	6	28		SBP, DBP, HR
	Wu et al. (1999)	CG: 64.0; CO: 68.0	AD	0	9	0	9		Growth hormone mRNA expression from B cells and T cells
	Glaser et al. (1998)	CG: 73.0; CO: 71.5	AD or other dementia	15	39	20	49		Four-fold antibody response to flu vaccine; baseline antibody levels
	Atkinson (1995)	CG: 67.2; CO: 68.1	AD	23	52	23	57	Medication use	Weight change
3	Kiecolt-Glaser et al. (1995)	CG: 62.3; CO: 60.4	Dementia	0	13	0	13		IL-1b mRNA expression in response to lipopolysaccharide, IL-1b mRNA expression in response to TNF, IL-1b mRNA expression in response to GM-CSF, number of days of wound healing[a]
4	Irwin et al. (1991)	CG and CO: 71.3	AD	18	30	6	11		EPI, NEPI, neuropeptide Y, NKA
5	Irwin et al. (1997)	CG: 71.0; CO: 69.6	AD	43	57	14	19		ACTH, beta-endorphin, cortisol, prolactin, EPI, NEPI, neuropeptide Y, NKA
	Mills et al. (1997)	CG: 73.5; CO: 74.0	AD	6	21	8	2		CD4, CD8, CD16, cortisol, EPI, NEPI, beta-receptor sensitivity, beta-receptor density, forskolin stimulation, SBP, DBP, weight
	Patterson et al. (1998)	CG: 63.7; CO: 61.2	AD	68	106	71	69	Number of physical symptoms	
	Shaw et al. (1997)	CG: 70.6; CO: 69.7	AD	53	97	22	24	Medication use, hospitalization, objective health rated by nurse	
	Shaw et al. (1999)	CG: 70.5; CO: 70.2	AD	51	93	24	23	Antihypertensive medication use	SBP, DBP, BMI

(*table continues*)

Table 2 (*continued*)

Sample	Report	Mean age	Care recipients	CG M	CG W	CO M	CO W	Self-reported measures	Physiological measures
6	Picot et al. (1997)	CG: 60.8; CO: 55.5	AD and other chronic conditions	0	18	0	24	Number of chronic conditions, antihypertensive medication use	SBP, DBP, HR
7	Pomara et al. (1989)	CG: 63.6; CO: 64.5	AD	0	5	2	2		CSF, GABA
8	Reese et al. (1994)	CG: 56.3; CO: 60.9	AD, stroke	16	34	8	17		NK cell, lymphocyte, CD3, CD4, CD8, CD4/CD8
9	Vedhara et al. (1999)	CG: 73.0 (*Mdn*); CO: 68.0 (*Mdn*)	AD, dementia, Parkinson's disease	24	26	31	36		Salivary cortisol, IgG responses to vaccines
10	Scanlan et al. (1998)	CG: 69.8; CO: 69.1	AD	29	52	25	57	Number of chronic conditions	CD4, CD8, CD4:CD8 ratio, BMI
	Vitaliano, Russo, et al. (1993)	CG: 69.4; CO: 68.5	AD	30	52	30	48	Antihypertensive medication use	SBP, DBP, HR
	Vitaliano et al. (1995)	CG: 69.8; CO: 69.1	AD	36	60	29	62		Total cholesterol, LDLC, HDLC, triglycerides, BMI
	Vitaliano, Scanlan, Krenz, & Fujimoto (1996)	CG: 69.8; CO: 69.1	AD	25	48	20	49		Insulin, glucose, lipids, BMI
	Vitaliano, Scanlan, Krenz, Schwartz, & Marcovina (1996)	CG: 69.8; CO: 69.1	AD	29	52	26	60	Antihypertensive medication use	BMI, lipids
	Vitaliano, Scanlan, Ochs, et al. (1998)	CG: 69.8; CO: 69.1	AD	27	53	26	59		NKA
	Vitaliano, Scanlan, Siegler, et al. (1998)	CG: 69.8; CO: 69.1	AD	24	47	21	49		Metabolic syndrome, SBP, DBP, insulin, glucose, BMI, HDLC, triglycerides
	Vitaliano et al. (1999)	CG and CO: 69.5	AD	29	51	25	60		NKA
11	Almberg et al. (1998)	CG: 66.6; CO: 68.8	Dementia	15	37	23	43	Health problems in a burden questionnaire, coded as yes/no	
12	Baumgarten et al. (1992)	CG: 66.7; CO: 60.4	Dementia	40	63	46	69	Global self-reported health, medication use, number of physical symptoms	
	Baumgarten et al. (1997)	CG: 63.2% above 65; CO: 44.2% above 65	Dementia	33	62	41	63	Number of chronic conditions; medical record of number of physician visits	
13	Grafstrom et al. (1992)	—	Dementia	35	75	73	159	Medication use, number of physician visits, percentage having health worse than expected	
14	Haley et al. (1987)	CG: 57.8; CO: 53.4	Dementia	12	32	12	32	Number of physical symptoms (PILL), global self-reported health, number of physician visits, number of current prescription medications, number of chronic conditions, health status	

Table 2 (*continued*)

Sample	Report	Mean age	Care recipients	CG M	CG W	CO M	CO W	Self-reported measures	Physiological measures
15	Haley et al. (1995)	CG: 58.7; CO: 56.4	Dementia	60	115	58	117	Cardiovascular and respiratory symptoms (Cornell Medical Index); global self-reported health; number of physician visits, hospitalizations; medication use	
16	Lorensini & Bates (1997)	CG: 31.2% under 50; CO: 42.5% under 50	Dementia	21	64	6	41	Number of days in bed or hospital in past 12 months, number of physician visits in past 12 months	
17	McNaughton et al. (1995)	CG: 71.1; CO: 70.4	AD	$N = 89$[b]		$N = 31$[b]		Number of physical symptoms (Interim Medical Survey); objective health (ratings based on number of physician visits, medication use, number of physical symptoms, hospitalizations)	
18	O'Reilly et al. (1996)	CG: 56.5; CO: 56.4	Parkinson's disease	55	99	47	77	Number of chronic illnesses; number of physician visits, hospitalizations; medication use	
19	Rose-Rego et al. (1998)	CG: 70.4; CO: 72.5	AD	38	61	39	74	Global self-reported health	
20	Wright (1994)	CG: 69.0; CO: 68.6	AD	6	24	4	12	Multilevel Assessment Inventory (MAI; self-rated health; number of physician visits in the past year, days of hospitalization in the past year, medications taken per day; and ratings of heart and circulatory problems make up combined score; a maximum of 27 indicates perfect health)	
	Wright et al. (1999)	CG: 67.2; CO: 63.9	AD, stroke	17	11	9	5	Global self-rated health; MAI	
21	Fuller-Jonap & Haley (1995)	CG: 74.5; CO: 74.1	AD	52	0	53	0	Global self-rated health, number of physician visits; cardiovascular and respiratory symptoms (Cornell Medical Index)	
22	J. J. McCann (1991)	CG: 67.5; CO: 67.2	AD, Multi-infarct, and unspecified dementia	0	34	0	33	Global self-rated health; number of physician visits, days of illness, chronic illnesses, medications	Number and percentage of total lymphocyte, CD3, CD4, CD8, CD56, and B cells; delayed skin hypersensitivity
23	Giefer (1994)	CG and CO: 75.0 (*Mdn*)	Dementia and frail older adults	14	26	14	24		IgG profile (IgG, IgM, IgA)

Note. A dash indicates that the data could not be computed because same or all of the information was unavailable. CG = caregiver; M = men; W = women; CO = control (noncaregiver); AD = Alzheimer's disease; NK = natural killer; CD = cluster designation; EBV = Epstein Barr virus; VCA = virus capsid antigen; IgG = immunoglobulin G; ConA = concanvillan A; PHA = phytohemagglutinin; NKA = natural killer cell activity; rIFN = interferon receptor; rIL-2 = interleukin 2 receptor; BMI = body mass index; HSV-1 = herpes simplex virus Type 1; ELISA = enzyme linked immunosorbent assay; HAI = hemaglutinin inhibition assay; IL-1b = interleukin-1b; IL-6 = interleukin 6; IL-2 = interleukin 2; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate; TNF = tumor necrosis factor; GM-CSF = granulocyte-macrophage colony stimulating factor; EPI = epinephrine; NEPI = norepinephrine; CSF = cerebrospinal fluid; GABA = gamma-aminobutyric acid; LDLC = low-density cholesterol; HDLC = high-density cholesterol; PILL = Pennebaker Inventory of Linguid Languidness; IgM = immunoglobulin M; IgA = immunoglobulin A.

[a] This effect size was not included in some of the meta-analyses. [b] Both men and women are included in this number because the original study did not stratify the category by sex.

higher score corresponded to poorer health. Other reports used items such as "increase in health problems" and "percentage who had worse health than expected" or composite health scores from the Multilevel Assessment Inventory (Lawton, Moss, Fulcomer, & Kleban, 1982) and the Duke University Center for the Study of Aging and Human Development (1978).

2. Number of chronic conditions was assessed in seven samples ($n = 476$ caregivers, $n = 461$ noncaregivers). Chronic illnesses were measured by checklists. One example is the Health Status Questionnaire (Belloc, Breslow, & Hochstim, 1971).

3. Number of physical symptoms was assessed in eight samples ($n = 742$ caregivers, $n = 649$ noncaregivers). Measures included the Pennebaker Inventory of Linguid Languidness (Pennebaker, 1982), the Cornell Medical Index, and the Interim Medical Survey.

4. Medication use was examined in 10 samples ($n = 941$ caregivers, $n = 960$ noncaregivers). This included the number of medications or percentage of people taking a medication. As this is a review of physical health, we focused on somatic medications.

5. Health service utilization was assessed in 11 samples ($n = 1{,}002$ caregivers, $n = 961$ noncaregivers). This included number of clinic visits in the past 3 or 6 months, days in hospital, percentage of people who visited a physician more than once, and percentage of people hospitalized.

Six physiological health categories. Here we only present information on the measures used in each category and not the rationales, as they are provided in Table 1.

1. Antibodies were assessed in four samples ($n = 175$ caregivers, $n = 187$ noncaregivers), namely, immunoglobulin G (IgG) response to herpes simplex virus (HSV) Type 1 and vaccination, Epstein Barr virus (EBV) virus capsid antigen IgG titers, and immunoglobulins.

2. Other functional immune measures were examined in six samples ($n = 308$ caregivers, $n = 216$ noncaregivers). The OSU's second and third samples examined T-cell proliferation responses to mitogens (concanvillan A, phytohemagglutinin), responses to cytokine stimulation (NKA in response to interferon-receptor, lymphokine activated killing in response to interleukin 2 receptor), cytokine responses (interleukin-1b [IL-1b], etc.), IL-1b mRNA in response to lipopolysaccharide, tumor necrosis factor, granulocyte-macrophage colony-stimulating factor, and delayed skin hypersensitivity from antigen and induration scores.

3. Enumerative immunity was examined in six samples ($n = 266$ caregivers, $n = 226$ noncaregivers), namely, lymphocyte counts and percentages of different subsets (e.g., cluster designation [CD]4, CD8).

4. Stress hormones and neurotransmitters were examined in five samples ($n = 176$ caregivers, $n = 119$ noncaregivers). Measures included ACTH, epinephrine, norepinephrine, cortisol, prolactin, neuropeptide Y, gamma-aminobutyric acid (GABA), beta-receptor sensitivity and density, forskolin stimulation, and growth hormone from B and T cells.

5. Cardiovascular measures were examined in four samples ($n = 217$ caregivers, $n = 161$ noncaregivers). These included systolic and diastolic blood pressure and heart rate.

6. Metabolic measures were examined in five samples ($n = 309$ caregivers, $n = 256$ noncaregivers). These included body mass, weight, cholesterol, insulin, glucose, and transferin.

The speed of healing in response to a standardized skin wound has been used to assess a caregiver's ability to heal damaged tissue. It is dependent on interactions of immune, hormonal, and nutritional factors. Because it was only examined in one sample (Kiecolt-Glaser, Marucha, Malarkey, Mercado, & Glaser, 1995), it could not be included in a category by itself, but it was used to calculate global relationships.

Coding Procedures and Rater Reliability

Jianping Zhang and James M. Scanlan examined the 45 reports for codeable data, such as means, *t* tests, and so on. Data were included if information was available to transform a contrast to the point-biserial correlation (r_{pb}). We used the point-biserial correlation as the effect size because it reflects the observational nature of caregiver research and it is easy to understand and interpret. In each computation, we coded noncaregivers as 0 and caregivers as 1. As such, larger point-biserial correlations suggested greater health risks for caregivers. A total of 172 computable point-biserial correlations were obtained. Rater reliability was .92 for two raters across five reports with self-reported measures and six reports with physiological measures.

Analyses Used to Calculate Within-Sample Point-Biserial Correlations

Lipsey and Wilson (2001) provided the main source for the point-biserial correlation calculations. Below we discuss the decision rules used for their derision.

1. If the mean, standard deviation, sample size, or percentage was included for each measure in each group but the article did not report a statistical test for the difference between caregivers and noncaregivers, we computed a *t* test or chi-square test for independent samples using the pooled variance. The r_{pb} was transformed from *t* according to standard formulae.

2. If the tests and degrees of freedom were included, point-biserial correlations were computed using the above transformation regardless of whether the means and standard deviations were reported. This was done because in cases of missing data or outliers, the sample used to calculate the statistical test might not have been the same as the one reported in the descriptive results.

3. If a probability value was reported without a test value and the sample sizes were known, we estimated the value using a reverse distribution function and obtained the point-biserial correlation.

4. If an article reported that a difference between groups was not significant, but it did not provide a test value, probability value, or means and standard deviations, we recorded the comparison as *nsnd* (nonsignificant, no data). In such cases, we calculated the average point-biserial correlations twice for that sample and category, namely, without the nsnd and by setting the nsnd values to zero. This allowed us to observe how nonsignificant findings influenced the average point-biserial correlations.

5. In one article (Mills et al., 1997), two groups of caregivers were available. In this case, we first averaged the groups and then computed the point-biserial correlations.

6. Some articles included, not only groups of caregivers whose care recipients were living at home, but also other types of caregivers. The latter included former caregivers (Glaser, Kiecolt-Glaser, Malarkey, & Sheridan, 1998), bereaved caregivers (Cacioppo et

al., 1998; Esterling, Kiecolt-Glaser, Bodnar, & Glaser, 1994; Esterling, Kiecolt-Glaser, & Glaser, 1996; Lorensini & Bates, 1997; Wright, Hickey, Buckwalter, Hendrix, & Kelechi, 1999), caregivers of care recipients in nursing homes (Wright et al., 1999), and caregivers using adult day care (Lorensini & Bates, 1997). When the data were stratified, we used only current caregivers, caregivers caring for care recipients in their homes, or caregivers that were not using adult day care.

7. In the few samples with repeated measures data, we used the first timepoint to compute point-biserial correlations because this was commensurate with data from the vast majority of other samples.

8. If the same measure was used across overlapping reports, the point-biserial correlations were averaged and represented only once for that sample. The mean of the resulting means was then obtained. For example, NKA was used in four samples with seven reports. As such, it was first averaged across the reports in each sample and then the resulting four sample means were averaged.

9. For each physiological measure we had to determine the direction of its most common relationship with illness. In doing so we recognized that although indicators such as obesity and high glucose are usually associated with negative health outcomes, very low body weight and glucose might also result from starvation. Moreover, high NKA and CD4 are usually associated with better health, but there are rare diseases in which they may be elevated. In almost all cases, the most common association was for higher values with greater health risk, but for some immune markers and high-density lipoproteins, lower values indicated more risk. In these cases, we reversed the coding so that higher values represented more risk.

Analyses Used to Assess Central Tendencies, Variability, Significance, and Moderators

Random-effects and fixed-effects models. Inferences about central tendencies relative to several sources of variation can be made using random-effects or fixed-effects models. The random-effects model is usually used when the goal of a meta-analysis is to generalize the findings beyond the collection of observed or identical studies. Greater generalizability is achieved by incorporating between-studies variability into error estimates, variance, and statistical tests (Hedges & Vevea, 1998; Lipsey & Wilson, 2001). The fixed-effects model is often used when one's goal is to make inferences to the observed or identical studies, except for random error sampling of participants into each study. Although the random-effects model is more generalizable, the costs of applying it are generally broader confidence intervals and less powerful test results when making conditional inferences (Hedges & Vevea, 1998). Alternatively, when heterogeneous effect sizes exist, generalizing the results of fixed error models beyond the studies used is problematic because systematic variability is unexplained. Here, the point-biserial correlations were assumed to be heterogeneous across samples when the Q statistic exceeded the critical value of the chi-square, with $k - 1$ degrees of freedom. In such cases, we examined potential outliers (Shadish & Haddock, 1994). Because the fixed-effects model also allows important inferences, we used both approaches. However, we only report fixed error results when they are significant and the random error results are not.

Mean point-biserial correlations. Two types of tests were conducted—those in which mean point-biserial correlations were compared with zero and tests of contrasts, in which mean point-biserial correlations were compared with each other. To calculate a mean point-biserial correlation, all r_{pb}s were first transformed to Fisher's Z_r. Each sample was then weighted by its appropriate mean weights (Shadish & Haddock, 1994). If a sample generated one report, the function of the sample size was used to weight the point-biserial correlation in the composite of point-biserial correlations from that category. If a sample generated multiple reports using the same measure, the sample sizes in the reports were first averaged to weight the point-biserial correlation for that measure. To calculate the grand mean point-biserial correlation of the 23 samples, we computed the unweighted mean point-biserial correlation within each sample. The 23 mean point-biserial correlations were then each weighted by a function of their sample size (mean n was used for the OSU, UW, and UCSD samples) and used to compute the grand mean. When computing the point-biserial correlations for the five reported health categories or the six physiological categories, we first averaged across point-biserial correlations within each sample in that grouping (i.e., $k = 17$ and 12, respectively). These values were then weighted by their sample size functions, and their averages were obtained across the samples. This was also done for the means of the 11 health categories. In all cases, the means of the point-biserial correlations were computed from Lipsey and Wilson's (2001) formulae using the SPSS macro procedure. For the random error model, a test was used that assumes this model (Bryk, Raudenbush, & Congdon, 1996; Shadish & Haddock, 1994). Contrast tests were done for reported health versus physiological measures; global self-reported health versus utilization, medications, and chronic illnesses; stress hormones versus cardiovascular and metabolic measures; antibodies versus enumerative measures; and antibodies versus other functional immune measures.

Analyses Used to Examine Data Censoring and Data Interpretation

We examined data censoring in two ways. First, we compared the mean point-biserial correlations of published and unpublished studies. Second, we used the trim and fill procedure. This method is useful when the primary goal of a meta-analysis is to establish the existence of a relationship between two variables. In such cases it is important to examine the robustness of findings relative to all possible sources of data censoring. The trim and fill method (Duval & Tweedie, 2000) first develops a funnel plot of studies, defined by the effect sizes on the x axis and the standard errors or sample sizes on the y axis. Once the plot is created, studies from the asymmetric outlying part of the funnel are trimmed. The symmetric remaining studies provide a "more accurate" effect size estimate. Correct calculation of the variance for the pooled estimate requires that the trimmed studies be replaced and their apparent missing counterparts on the funnel plot be filled by inputting values. This is based on the assumption that the sides of the funnel plot should be a mirror image of each other (Sutton, Song, et al., 2000). The fill step allows for adjusted overall confidence intervals to be calculated. Funnel plots may be asymmetric from factors other than publication bias. These include study quality, different outcome measures, and so forth. Therefore, changed results based on inputted values should be interpreted with caution (Sutton, Duval, Tweedie, Abrams, & Jones, 2000). When a mean effect size withstands this procedure it has enhanced credibility. Here we used the STATA macro procedure, METATRIM (Steichen, 2001), which employs the methods of Duval and Tweedie (2000). Finally, to examine the meaning and interpretability of the grand means of the point-biserial correlations, we assessed study-level effect sizes. This was done by correlating the point-biserial correlations for different categories of health measures across those studies that assessed more than one health indicator.

Results

Across the 23 samples ($n = 3{,}072$), 18 were from North America, 4 were from Europe, and 1 was from Australia. The grand mean for age was 65.0 years, and the range of the age means was 55 to 75 years. The median percentage of women was 65.1, and the range was 0% to 100%. The median number of non-White participants was 7.4%, with the sample percentages varying from 0 to 100. Overall, there were 1,594 caregivers and 1,478 noncaregivers

that were group matched on age and sex in the 23 observational studies. The mean ages were 65.6 years ($SD = 5.9$) for caregivers and 64.6 years ($SD = 6.4$) for noncaregivers. The median percentage of women was 65.0 for caregivers and 65.2 for noncaregivers.

Point-Biserial Correlations of Caregiving With Indicators of Physical Health

Grand means for all studies, self-reported studies, and physiological studies. There were 172 point-biserial correlations that could be calculated across the 45 reports (13 from dissertations and 159 from articles). Forty-one nonsignificant comparisons were also reported (or 19% of 213 comparisons), with insufficient data to calculate point-biserial correlations. For the 23 samples, the overall grand mean was significant when the nonsignificant values were set to zero ($r_{pb} = .10$, $p < .01$), and it was also significant when these values were ignored ($r_{pb} = .12$, $p < .01$). The 17 samples that examined the five self-reported health categories generated 7 to 14 contrasts in each category. A total of 57 contrasts were reported, of which 53 point-biserial correlations could be calculated. For the self-reported health categories the mean was also significant ($r_{pb} = .10$, $p < .01$), both with and without nonsignificant values set to zero. Caregivers reported more health problems than did noncaregivers. The 12 samples that examined the six physiological categories contained 14 to 56 contrasts. Of the 155 contrasts (154 + 1 contrast for wound healing), 118 point-biserial correlations could be calculated. The mean was significant ($r_{pb} = .11$, $p < .05$) when nonsignificant values were set to zero, as well as when they were ignored ($r_{pb} = .15$, $p < .01$). These results suggest that caregivers had greater potential illness risks than did noncaregivers.

Mean point-biserial correlations and variability within subcategories. For each sample (row) of Table 3, we provide point-biserial correlations for the five self-reported health categories that were examined. The last three rows include the mean point-biserial correlations using the random error model, without and with the nsnd results set to zero, and the number of point-biserial correlations used to calculate the means and, in parentheses, the number of nsnd results in each health category. Table 4 is similar to Table 3, but it contains the physiological results.

Table 5 provides a summary of 14 groups of point-biserial correlations. These include the set of all point-biserial correlations calculated, the point-biserial correlations for all self-reported health measures, the point-biserial correlations for all physiological measures, and the point-biserial correlations for the 11 subcategories. For each group, the table includes columns containing (a) category name; (b) number of independent samples (k); (c) sample sizes for caregivers and noncaregivers (controls); (d) mean point-biserial correlation for the random-effects model ignoring nsnd, with significance levels, 95% confidence intervals, and Q statistic; (e) mean point-biserial correlations for the random-effects model with nsnd results set to zero, with significance levels, 95% confidence intervals, and Q statistic; and (f) trim and fill estimates of the mean point-biserial correlation with nsnd values set to zero.

From the table, one can see that in eight categories there was either no difference or a minor difference between the mean point-biserial correlations for the calculations in which nsnds were ignored versus the calculations in which they were set to zero. In other categories, the drop in the mean point-biserial correlation was more substantial when zeros were substituted for nsnds. These included global self-reported health (16% drop), functional cellular immunity (23% drop), all physiological samples (27% drop), stress hormones (28% drop), and enumerative immunity (42% drop). This last difference is not surprising because 25 of the 56 point-biserial correlations in this category were nsnd. To be conserva-

Table 3
Point-Biserial Correlation Coefficients for Self-Reported Health Measures

Sample	Report	Global self-reported health	Chronic illnesses	Physical symptoms	Medication use	Health service utilization
1	Almberg et al. (1998)	.28				
2	Baumgarten et al. (1992, 1997)	.28	.04	.25	.38	.02
3	Grafstrom et al. (1992)	.13			.05	.07
4	Haley et al. (1987)	.18	.25	.11	.22	.19
5	Haley et al. (1995)	.09		−.02	−.03	−.03
6	Lorensini & Bates (1997)					−.09
7	McNaughton et al. (1995)			.07		
8	O'Reilly et al. (1996)		−.08		.11	−.01
9	Rose-Rego et al. (1998)	.22				
10	Wright (1994), Wright et al. (1999)	.09				
11	Fuller-Jonap & Haley (1995)	—		.12		—
12	Kiecolt-Glaser et al. (1987)	—				
13	OSU second sample		.12	.11	.04	.29
14	UCSD second sample			.05	.06	.08
15	Picot et al. (1997)		.11		.04	
16	UW group		.24		.01	
17	J. J. McCann (1991)	.25	.12	.18	.36	.21
Mean r_{pb}						
Random-effects model without nsnd		.18	.11	.10	.12	.06
Random-effects model with nsnd at 0		.16	.11	.10	.12	.05
Number of r_{pb}s (nsnd)		10 (2)	7 (0)	13 (0)	11 (0)	12 (2)

Note. Point-biserial correlations (r_{pb}s) are unweighted. A dash indicates that the value could not be computed because it was recorded as nonsignificant, with no data (nsnd). OSU = Ohio State University. UCSD = University of California, San Diego. UW = University of Washington.

Table 4
Point-Biserial Correlation Coefficients for Physiological Measures

Sample	Report	Functional cellular immunity	Antibodies	Enumerative immunity	Stress hormones	Cardiovascular	Metabolic
1	Kiecolt-Glaser et al. (1987)		.26	.27			−.13
2	OSU second sample	.29	.17	.07	.46	—	.10
3	Kiecolt-Glaser et al. (1995)	.20					
4	Irwin et al. (1991)	—			.32		
5	UCSD second sample	−.14		.07	.03	−.03	−.19
6	Picot et al. (1997)					−.03	
7	Pomara et al. (1989)				.89		
8	Reese et al. (1994)			.03			
9	Vedhara et al. (1999)		.08		.23		
10	UW group	−.05		.03		−.01	.01
11	Giefer (1994)		.14				
12	J. J. McCann (1991)	.41		.32			.15
Mean r_{pb}							
Random-effects model without nsnd		.13	.15	.12	.32	−.02	−.01
Random-effects model with nsnd at 0		.10	.15	.07	.23	−.02	−.01
Number of r_{pb}s (nsnd)		23 (3)	13 (1)	31 (25)	17 (3)	11 (5)	23 (0)

Note. Point-biserial correlations (r_{pb}s) are unweighted. A dash indicates that the value could not be computed because it was recorded as nonsignificant, with no data (nsnd). OSU = Ohio State University. UCSD = University of California at San Diego. UW = University of Washington.

tive, we focus here on results with nsnd coded as zero (see *M* and *Q* columns for weighted r_{pb} with nsnd, Table 5).

Across categories, the largest point-biserial correlations were for stress hormones ($k = 5$; $r_{pb} = .23$, $p < .05$), global self-reported health ($k = 10$; $r_{pb} = .16$, $p < .01$), and antibodies ($k = 4$; $r_{pb} = .15$, $p < .01$). In all cases, caregivers reported greater health problems and/or had greater potential risks than did noncaregivers. For health service utilization, chronic illnesses, metabolic, and cardiovascular categories, the point-biserial correlations for the random-effects model were not significant, but the point-biserial correlations for the fixed-effects model were significant for chronic illnesses ($k = 7$; $r_{pb} = .08$, $p < .05$) and health service utilization ($k = 11$; $r_{pb} = .04$, $p < .05$). Fixed-effects models are difficult to interpret with heterogeneous effect sizes, which was true for chronic illnesses. However, when an outlier (−.075 for O'Reilly, Finnan, Allwright, Smith, & Ben-Shlomo, 1996) was dropped, the measure of heterogeneity became nonsignificant ($Q = 4.93$, $p = .33$) and the point-biserial correlation became .14 ($p < .01$; $k = 6$). O'Reilly et al. (1996) examined caregivers of Parkinsonian patients, but the other samples examined AD caregivers. It has been shown that when distress is not controlled (as in O'Reilly et al., 1996), caregivers of Parkinson's patients report fewer health problems than caregivers of persons with AD (Hooker, Monahan, Bowman, Frazier, & Shifren, 1998).

Table 5
Mean Random-Effects Model Point-Biserial Correlations (r_{pb}s), Q Statistics, and Trim and Fill Estimates for Each Category

		n		Weighted r_{pb} without nsnd			Weighted r_{pb} with nsnd			
Category	*k*	CG	CO	*M*	95% CI	*Q*	*M*	95% CI	*Q*	Trim and fill r_{pb}
All samples	23	1,594	1,478	.12**	.07, .17	45.09**	.10**	.05, .15	38.96*	.09**
All self-report samples	17	1,405	1,388	.10**	.05, .15	23.23	.10**	.05, .14	23.72	.10**
All physiological samples	12	601	461	.15**	.05, .25	25.78**	.11*	.02, .19	19.02	.11*
Global self-reported health	10	717	879	.19**	.12, .25	8.60	.16**	.10, .23	13.41	.16**
Chronic illnesses	7	476	461	.10	−.00, .21	14.18*	.11	−.00, .21	14.18*	−.02
Physical symptoms	8	742	649	.10**	.03, .17	10.97	.10**	.03, .17	10.97	.03
Medication use	10	941	960	.12*	.03, .21	34.67**	.12*	.03, .21	34.67**	.12*
Health service utilization	11	1,002	961	.06	−.01, .14	17.77*	.05	−.01, .12	18.14	.05
Functional cellular immunity	6	308	216	.13	−.09, .34	20.04**	.10	−.08, .27	19.42**	.10
Antibodies	4	175	187	.15**	.05, .25	1.48	.15**	.04, .25	1.43	.15**
Enumerative immunity	6	266	226	.12*	.02, .23	6.51	.07	−.02, .16	3.42	.07
Stress hormones	5	176	119	.32**	.08, .52	13.42**	.23*	.00, .43	11.71*	.23*
Cardiovascular	4	217	161	−.02	−.13, .10	0.02	−.01	−.12, .09	0.04	−.01
Metabolic	5	309	256	−.01	−.14, .12	8.56	−.01	−.14, .12	8.56	−.01

Note. *k* = number of independent samples; CG = caregiver; CO = control (noncaregiver); nsnd = nonsignificant without sufficient information to compute effect sizes; CI = confidence interval; *Q* = measure of heterogeneity.
* $p < .05$. ** $p < .01$.

Contrast Tests

As we noted at the beginning of our article, there are reasons to examine three contrasts. These include the relationships of caregiving with global health versus other self-reported health, stress hormones versus cardiovascular and metabolic measures, and antibodies versus other immunologic measures. In performing these tests we eliminated the problem of nonindependence within a contrast level, such as for other self-reported health (utilization, medications, and illnesses) by averaging over the point-biserial correlations for the multiple correlated measures within each sample. However, although the point-biserial correlations were independent within contrast levels, they were not all independent across contrast levels, for example, global versus other self-reported health. In such cases, the use of independent tests across correlated samples made our findings more conservative. Our results suggest that the point-biserial correlation for global self-reported health (.16) was greater than that for the combination of utilization, medications, and illnesses (.06), $Q(1) = 8.98$, $p < .01$. The point-biserial correlation for stress hormones (.19), using the random-effects model, was not greater than that for cardiovascular and metabolic measures (−.01), $Q(1) = 3.50$, $p < .06$. However, under the fixed-effects model, the point-biserial correlation for stress hormones (.17) was greater than that for cardiovascular and metabolic measures (.00), $Q(1) = 6.52$, $p < .01$. The point-biserial correlation for antibodies for the fixed-effects model (.15) was also greater than that for other functional immune measures (−.01), $Q(1) = 4.70$, $p < .03$, but the point-biserial correlations for antibodies, for the random-effects model (.15) and for other functional immune measures (.01), $Q(1) = 2.80$, $p < .10$, were not different. Finally, despite an almost 2:1 ratio in magnitude, the point-biserial correlations for antibodies and enumerative immunity were not different.

Tests of Demographic Variables as Moderators

To perform these analyses, we first recorded the number of samples that assessed each potential moderator. Sex, age, and relationship to the care recipient were reported in enough studies to meaningfully allow such analyses.

Tests of sex as a moderator. We examined sex as a moderator using several types of contrasts. These included (a) comparisons of men and women caregivers (r_{pb}s of sex with health indicators in caregivers), (b) comparisons of caregivers and noncaregivers separately for men and women (r_{pb}s of caregiver status with health indicators stratified on sex), and (c) comparisons of the point-biserial correlations obtained for men and women in (b) above. In the first comparisons, which were similar to correlating percentages of women (or men) in each study with the obtained point-biserial correlations, we were cognizant of the fact that the base rates of certain health indicators may differ across sex. For example, on average, men have higher systolic blood pressure, and women have higher high density lipoprotein levels and self-reported health problems. As such, the latter tests are better indicators of sex's moderation of caregiving with health. Also, studies that have compared male caregivers with male noncaregivers may differ in inclusion criteria and assay assessments from studies that have compared female caregivers with female noncaregivers. For this reason, the comparisons in (c) above compared the point-biserial correlations in studies that had simultaneously examined differences in caregivers and noncaregivers in both men and women. These analyses had the effect of first controlling for sex differences across samples by stratifying on sex and then controlling for different inclusion criteria and assay assessments across studies by requiring the same studies across each contrast. Although such criteria limited the number of studies that could be used in each comparison, this resulted in less confounding from sources other than sex. Using this approach, global health was assessed in enough studies to be a separate category, but we had to collapse the physiological measures into immunologic and hormone–cardiovascular–metabolic (HCM) categories.

However, the comparisons of male caregivers with female caregivers did allow for sex comparisons of three additional studies (Gallant & Connell, 1997; Neundorfer, 1991; Sparks, Farran, Donner, & Keane-Hagerty, 1998). These were not included in the 45 reports cited above because they did not contain noncaregivers.

Table 6 contains the point-biserial correlations using the random-effects model for the analyses that examined sex moderation. In these analyses women were coded as 1, and men were coded as 2. Hence, positive point-biserial correlations meant that the observed values for male caregivers were greater than those for female caregivers, and negative point-biserial correlations meant the opposite. According to this framework, female caregivers ($n = 500$) reported poorer global health than did male caregivers ($n = 262$; $r_{pb} = -.10$, $p = .01$) for the five available samples (Gallant & Connell, 1997; Grafstrom, Fratiglioni, Sandman, & Winblad,

Table 6
Point-Biserial Correlations (r_{pb}s) for Analyses of Sex Moderation for Global Self-Reported Health and Physiological Measures

	Global self-report		HCM		Immunologic	
Comparison	r_{pb}	n	r_{pb}	n	r_{pb}	n
CG men vs. CG women	−.10**	762	.07	214	−.02	181
CG men vs. NCG men	.15	222	.11	112	−.06	112
CG women vs. NCG women	.25**	450	−.01	186	−.05	186

Note. A positive r_{pb} suggests that the observed values of men were greater than those of women or that the observed values of caregivers (CGs) were greater than those of noncaregivers (NCGs); a negative r_{pb} suggests that the observed values of women were greater than those of men or that the observed values of NCGs were greater than those of CGs. HCM = hormone–cardiovascular–metabolic.
** $p < .01$.

1992; Neundorfer, 1991; Rose-Rego, Strauss, & Smyth, 1998; Sparks et al., 1998). For the HCM measures there was no difference in the 86 caregiver men and 128 caregiver women in the three available studies (Irwin et al., 1991; OSU second sample; UW sample; $r_{pb} = .07$, $p = .15$). However, the point-biserial correlation was positive, which contributed to the difference in the point-biserial correlations for global health (−.10) and HCM (.07), $Q(1) = 3.78$, $p = .05$. When comparing immunologic measures for caregiver men and women, the two studies (Irwin et al., 1991; UW sample; $n = 181$) yielded a point-biserial correlation of −.02.

In male caregivers versus male noncaregivers ($n = 222$), a nonsignificant result occurred for the random-effects model ($r_{pb} = .15$, $p = .13$) in the three studies that assessed global health (Almberg, Jansson, Grafstrom, & Winblad, 1998; Grafstrom et al., 1992; Rose-Rego et al., 1998). However, the result for the fixed-effects model was significant ($r_{pb} = .15$, $p = .05$), and the point-biserial correlations were homogeneous. Here, male caregivers reported worse global health than did male noncaregivers. Two studies compared male caregivers with male noncaregivers on HCM measures (Irwin et al., 1997; UW sample). In these, the relationship was not significant ($r_{pb} = .11$, $p < .12$) because the sample size was 112 and only two studies were available. Also, the mean for the HCM measures ($r_{pb} = .11$) was not significantly different from the mean for global health ($r_{pb} = .15$). When these same two studies were used to examine immune measures, the result was nonsignificant ($r_{pb} = -.06$).

Caregiver women reported worse global health than noncaregiver women in three studies ($n = 450$; Almberg et al., 1998; Grafstrom et al., 1992; Rose-Rego et al., 1998), with a mean point-biserial correlation of .25 ($p = .01$). Two studies of HCM measures (Irwin et al., 1997; UW sample; $n = 186$) yielded a nonsignificant result ($r_{pb} = -.01$, $p = .44$). The mean for global health ($r_{pb} = .25$) was greater than that for HCM measures ($r_{pb} = -.01$), $Q(1) = 2.90$, $p = .05$. The same two studies that assessed immunologic measures (Irwin et al., 1997; UW sample; $n = 186$) yielded a nonsignificant result ($r_{pb} = -.05$). The point-biserial correlations for the immunologic measures were not different for men (−.06) and women (−.05).

Tests of caregiver age and relationship to the care recipient as moderators. To examine whether age and relationship to the care recipient were associated with the obtained point-biserial correlations, we first determined whether they themselves were related. As noted for the contrast tests, we obtained independence of point-biserial correlations in these tests by first averaging over the point-biserial correlations within samples that had multiple measures—that is, all self-report measures or all physiological measures. Hence, when examining the relationships of point-biserial correlations with a potential moderator, each independent sample was represented by only one point-biserial correlation. Our analyses suggest that age was not related to the percentage of spouses across the 20 samples with such data ($r = .36$, $p = .11$). In the 15 studies that included age, the point-biserial correlations for self-reported health were higher in samples with older caregivers ($r = .49$, $p = .04$). For the physiological measures, no relationship was observed for age with the point-biserial correlations. Also, no associations occurred for reported health ($r = .07$, $k = 16$) and physiological measures ($r = -.23$, $k = 11$) with the caregiver's relationship to the care recipient (spouse vs. child caregiver).

Data Censoring and Interpretation

Unpublished dissertations versus published reports. Only one dissertation used an independent sample to examine reported health (J. J. McCann, 1991), so it was not tested for publication bias. Two samples used unpublished physiological data (Giefer, 1994; J. J. McCann, 1991) that were compared with samples with published physiological data. The point-biserial correlations were not different, $Q(1) = 0.07$, $p = .80$, namely, .11 and .14.

Trim and fill estimates. We performed the METATRIM procedure on all 14 groupings (see Table 5). In 11 of 14 categories, no studies were trimmed and filled. The 3 categories that changed involved the total set of studies, the chronic illnesses category, and the physical symptoms category. Across the total set of 23 point-biserial correlations, two studies were trimmed and filled, and the overall point-biserial correlation dropped by .01; however, it was still significant ($r_{pb} = .09$, $p < .05$). In the other two cases, the procedure trimmed and filled four studies each. In the chronic illnesses category ($k = 7$), the mean point-biserial correlation dropped from .11 to −.02 and became nonsignificant. Likewise, the mean point-biserial correlation for the physical symptoms category ($k = 8$) changed from .10 to .03 and became nonsignificant.

Study-level effect size. Intercorrelations of point-biserial correlations were calculated across measures in studies that had assessed health indicators in two or more categories. Some correlations were based on two or three studies, but we only interpreted those computed on four or more studies. Of these, nine pairs of correlations were computed across the self-report measures. The values ranged from .16 to .98 (median $r = .73$). Only three correlations could be computed on physiological measures in four or more studies. The three correlations ranged from .08 to .91 (median $r = .49$).

Discussion

To quantitatively review and critique the literature on caregiver health, we compared 1,594 caregivers of persons with dementia with 1,478 demographically similar noncaregivers. The point-biserial correlations were as follows: .09 for all health indicators ($k = 23$), .10 for reported health indicators ($k = 17$), and .11 for the physiological indicators ($k = 12$). Although these point-biserial correlations were significantly greater than zero, questions remain regarding their magnitudes and their clinical relevance. At first glance, it might appear that these are weak relationships, yet the decision to set nsnd point-biserial correlations to zero had some important effects in five categories. Enumerative immunity had a large number of nsnd values, and when these were set to zero, the point-biserial correlation dropped in magnitude by 42%, from .12 to .07. In other cases the point-biserial correlation dropped by 16% (global self-reported health), 23% (functional cellular immunity), 27% (all physiological samples), and 28% (stress hormones). However, even if one uses the estimates of the point-biserial correlations that include nsnd results set to zero, the means still have important implications because of the large number of important persons at risk. For example, the binomial effect size display (BESD; Rosenthal & Rubin, 1982) was used in the Physician's Clinical Aspirin Trial ($n = 22{,}000$) to show that a point-biserial correlation of .034 translated to 374 fewer myocardial infarctions in the physicians that ingested aspirin every other day

(Steering Committee of the Physicians' Health Study Research Group, 1988).

Using the BESD, the overall point-biserial correlation of .09 observed here translates to a 9% greater risk of health problems in caregivers than in demographically similar noncaregivers. This is important because there are more than 5 million caregivers of persons with dementia in the United States (American Association of Retired Persons, 1988) and at least another 5 million care recipients who may be affected if their caregivers become ill. These numbers are telling when one considers that caregivers had a 23% higher level of stress hormones compared with noncaregivers and that prolonged physiological reactions to elevated stress hormones, such as elevated blood pressure and glucose levels, can increase one's risk for hypertension and diabetes (see Table 1). The 15% poorer antibody production for caregivers may also be critical because their mean age was 65.1 years. Older adults are at higher risk for influenza, and their responses to vaccination are lower than younger adults' (Bernstein, Gardner, Abrutyn, Gross, & Murasko, 1998). Moreover, if older adults do not receive regular vaccinations, as many as 62% may have reduced antibodies to common pneumonia serotypes (Sankilampi, Isoaho, Bloigu, Kivela, & Leinonen, 1997).

Health Indicator Categories as Moderators of Caregiving With Health Outcomes

The fact that the point-biserial correlations for antibodies were higher than those for other functional immune measures is consistent with previous meta-analyses of immune measures with depression and stress (Herbert and Cohen, 1993a, 1993b).[3] Should we conclude, therefore, that caregiving does not influence other immunologic functions? To answer this question one must consider how these variables were measured and the designs of the studies in which they were used. First, functional immunity was primarily assessed using unchallenged assessments, yet caregivers have only been shown to have poorer functional responses than noncaregivers when NKA is stimulated (Esterling et al., 1994, 1996). Second, research on NKA in caregivers has ignored individual differences such as comorbidities, and comorbidities such as cancer history may moderate relationships of caregiving with NKA. For example, a history of cancer may predispose one to immunologic risk (Fawzy et al., 1993), and caregivers with cancer histories have lower NKA than do noncaregivers with cancer histories. In contrast, NKA does not differ in caregivers and noncaregivers free of cancer histories (Vitaliano, Scanlan, Ochs, et al., 1998).

The disregard for comorbidities may also have contributed to the small point-biserial correlations for cardiovascular and metabolic measures. In one study (Vitaliano, Russo, et al., 1993) no effect was observed for normotensive caregivers and normotensive noncaregivers in systolic blood pressure reactivity, but hypertensive caregivers showed greater reactivity than did hypertensive noncaregivers. Also, caregivers with CHD had higher levels on the metabolic syndrome—a linear combination of fasting glucose, insulin, lipids, mean arterial pressure, and obesity—than did noncaregivers with CHD; however, no difference occurred for caregivers and noncaregivers free of such disease (Vitaliano, Scanlan, Siegler, et al., 1998). For these reasons, relationships of caregiving with reactivity and the metabolic syndrome may be moderated respectively by hypertension and CHD. Unfortunately, in this meta-analysis we could not examine comorbidities because they were not reported or they were summarily excluded. Such exclusions may have limited researchers to those caregivers who were least likely to show dysregulation from chronic stress. This is ironic because spouse caregivers are typically aged 65 and over, and many are already ill when they enter research studies (among older adults, 40% have hypertension, 25% have heart disease, and 18% have diabetes; Centers for Disease Control and Prevention, 1998). These caregivers have not been adequately represented in research.[4] In summary, if caregivers are more likely to have major illnesses and to also have more health complications from the combination of comorbidities and caregiving, past selection criteria would have been biased against observing relationships with caregiving.

In this analysis the point-biserial correlation for global health was greater than that for the other reported health categories. We expected this would occur because, although illness reports are related to neuroticism and anxiety (Costa & McCrae, 1980; Watson & Clark, 1984), they are less associated with distress than is global health (Hooker & Siegler, 1992; Zhang, Vitaliano, Scanlan, & Savage, 2001). Also, global health is predictive of mortality (Idler, Kasl, & Lemke, 1990). When one considers that global health is highly related to strain and distress, this is consistent with the 63% higher death rate observed among strained caregivers than among noncaregivers in a 4-year follow-up study (Schulz & Beach, 1999).

Demographic Variables as Moderators of Relationships of Caregiving With Health Indicators

Sex. The sex results depended on the measures used. The point-biserial correlations for male versus female caregivers for global self-reported health (−.10) and HCM measures (.07) were significantly different because they were in opposite directions. Female caregivers reported more health problems, but they did not exhibit higher HCM risk. This pattern also occurred when differences in caregivers and noncaregivers were stratified on sex. For women, caregiving was not only more related to global self-reported health (.25) than it was to HCM measures (−.01), but the latter point-biserial correlation was minute. In contrast, for men, the HCM point-biserial correlation (.11) was neither negligible nor was it lower than that for global self-reported health (.15).

How should we interpret these results? Do the self-report results allow us to say that women are more vulnerable to caregiving than are men? There may be several problems with this interpretation. First, women report more health problems than men in many

[3] These results may be surprising because antibodies are variable in the face of antigens and lifetime viral exposure but other immune parameters are relatively constant, except when one is fighting illnesses. To reduce variability, however, researchers typically examine antigens to which the majority of older adults have had exposure (e.g., EBV). Moreover, antibody responses are also larger than is typically seen in other immune measures. Hence, one can see a four-fold increase in antibodies in response to vaccination but a 50% change in NKA in response to a stimulus or a 20% change in CD4 counts (in persons who are not HIV positive) would be unusual.

[4] Many researchers also excluded persons on medications, disallowing their interactions with stress and compromising external validity, given the large number of older adults on medications.

situations (Bosworth et al., 1999; Rahman et al., 1994; Ross & Bird, 1994). This may occur because women are more aware of their problems (Barsky, Peekna, & Borus, 2001) and are more likely to report them when they exist (King, Taylor, Albright, & Haskell, 1990). Therefore, the current findings may not be unique to caregiving. Second, global health is related to distress (Hooker & Siegler, 1992), and distress is higher in female caregivers than in male caregivers (Lutzky & Knight, 1994). As such, sex differences in distress may influence caregiver reports. Third, selection bias may have played a greater role in the results for male caregivers than for female caregivers. W. Stroebe and Stroebe (1987) have shown that differences in depression between widows and widowers who agreed to participate in face-to-face interviews were minimal; however, widowers who only agreed to do postal questionnaires reported significantly greater depression than did widows who only did postal questionnaires. Hence, selection bias in face-to-face research may work against finding sex differences.

A final issue involves the discrepancy between the magnitude and significance of the point-biserial correlations for caregivers and noncaregivers when stratified on sex. Although the HCM point-biserial correlation for female caregivers versus female noncaregivers was neither significant nor of meaningful magnitude (.01), this was not true for male caregivers versus male noncaregivers. The latter point-biserial correlation (.11) was as large as the point-biserial correlation for male caregivers versus female caregivers on global self-reported health ($-.10$, $p < .05$), but it was not significant because of the sample size. In fact, almost all physiological point-biserial correlations were minute, and the HCM point-biserial correlation for men was the only point-biserial correlation greater than .10 (see Table 6). Indeed, the sample sizes and number of studies that examined male caregivers versus male noncaregivers were among the smallest of all comparisons in this meta-analysis. The fact that the HCM point-biserial correlation for men is the largest physiological point-biserial correlation is consistent with research which has shown that men have greater stress responses to similar physiologic measures (Earle et al., 1999; Kirschbaum et al., 1999). Men also have greater negative responses to bereavement. Widowers have higher rates of physical disabilities (Goldman et al., 1995), diseases of the circulatory system (Joung, Glerum, vanPoppel, Kardaun, & Mackenbach, 1996), and mortality (Goldman et al., 1995) than do widows. Taylor et al. (2000) have argued that women's biopsychosocial adaptation to stress, in contrast to that of men, is to seek out relaxation and affiliation. This "may help to explain the seven-and-a-half non-specific years that women live longer than men . . . the tend-and-befriend pattern proposed here may reduce women's vulnerability to a broad array of stress-related disorders" (Taylor et al., 2000, p. 423). Tend-and-befriend stress reactions include nurturance, to protect the self and offspring and reduce distress, and the creation of social networks that facilitate nurturance.[5]

Caregiver age and relationship to the care recipient. In addition to sex, we examined the caregiver's age and relationship to the care recipient as potential moderators. Relationships of caregiving with self-reported health were greater for older participants. Although this supported the added vulnerability of older caregivers versus older noncaregivers, relative to younger caregivers versus younger noncaregivers, this was not observed for physiological measures. One methodological reason for this is that the range of age means was more restricted in samples with physiological measures than in samples with self-report measures (data not shown). A more substantive reason for this result may be that as age increases, increases occur in physical illnesses and disabilities (and in their variability; Rowe & Kahn, 1998), and these may be exacerbated by psychosocial distress, a strong correlate of self-reported health. The fact that the caregiver's relationship with the care recipient was not shown to be a moderator is difficult to interpret because of differences in the living arrangements of spouse versus child caregivers. In 9 of 11 samples, all caregivers were spouses, and 90% or more of the care recipients were living at home. In contrast, of the eight studies that mixed spouse and child caregivers, the percentage of care recipients at home varied from 0 to 70. The overlap in the caregiver's relationship with the care recipient and his or her place of residence may have affected the above result.

Meta-Analytic Issues and Limitations

As in all meta-analyses, we had to make a number of decisions about the criteria for choosing reports and how to combine reports once obtained. Clearly, these issues have effects on the heterogeneity of both the samples obtained and the aggregation of point-biserial correlations into subcategories. These decisions also affect the publication bias and external validity of the results.

Sources of data censoring and data interpretation. Meta-analyses of only published studies may yield higher point-biserial correlations and be positively biased in favor of significant results. As such, we supplemented the electronic search of published articles with hand searches and electronic searches of dissertations. The observed point-biserial correlation for dissertations (.15) exceeded the point-biserial correlation for articles (.10), which helped to counter the problem of publication bias. Also, the trim and fill procedure was used to examine the robustness of findings relative to all possible sources of data censoring. These include study quality and different outcome measures. Across all 14 groupings, only 3 categories were trimmed and filled, and 1 of these changed only slightly and remained significant. In the chronic illnesses and the physical symptoms categories, the procedure trimmed and filled four studies, and they each dropped dramatically in value and became nonsignificant. For this reason, the original results for chronic illnesses and physical symptoms must be interpreted with caution (Sutton, Duval, et al., 2000). In contrast, the findings in 12 of the 14 categories (see Table 5) withstood the exacting trim and fill procedure, and therefore the results of this meta-analysis have enhanced credibility (Sutton, Song, et al., 2000). Moreover, the median intercorrelations of the point-biserial correlations that assessed the interpretation of the study-level effect sizes suggest that there are consistencies across the different health measures.

[5] These data appear to be inconsistent with a review by Kiecolt-Glaser & Newton (2001), who concluded that "gender is an important moderator of the pathway from negative marital conflict behaviors to physiological functioning: This pathway is stronger for women than for men, and women's physiological changes following marital conflict show greater persistence than men's" (pp. 494–495). However, in the current article, most spouses were 60–70 years old, were probably married longer, and the reasons for their conflicts may have been different. Most AD caregivers do not blame their care recipients for their AD (Vitaliano, Young, Russo, Romano, & Magana-Amato, 1993). Hence, caregiver distress may be very different from conflicting marital interactions.

Inclusion criteria. To reduce heterogeneity and address the problem of combining studies with different samples, outcomes, and designs, the studies in this meta-analysis had to include (a) primarily caregivers of care recipients with dementia, (b) a noncaregiver comparison group, and (c) physical health measures. Although these criteria had advantages, we also recognize their disadvantages. Care recipients with AD, vascular dementias, and Parkinson's disease cluster together relative to other diseases, and these illnesses produce similar demand characteristics for caregivers (Vitaliano, Young, & Russo, 1991). However, the aggregation of care recipients across dementias may also result in heterogeneity because caregivers of patients with AD and vascular dementias experience different levels of burden at different times (Vetter et al., 1999). Such distinctions were not possible because in cases with multiple illnesses, the exact numbers were not specified or the samples were too small.[6] The decision to only use reports that included noncaregiver comparisons also had a disadvantage. Although it is accepted practice to limit conclusions about effect sizes to studies with comparison groups, this criterion restricted generalizability to such studies. Of all the reports that examined health problems in caregivers of care recipients with dementia, only 45 emerged when they were crossed with the terms *control*, *comparison*, or *noncaregivers*. Moreover, caregivers and noncaregivers were not demographically balanced on all potential confounds. Some studies (e.g., Kiecolt-Glaser et al., 1991) had higher levels of divorce and bereavement in noncaregivers than in caregivers, but these differences may have made their results conservative because such characteristics are related to poorer health (House, Landis, & Umberson, 1988). However, because these samples were not stratified, we could not compute point-biserial correlations separately for each marital status group.

Categorical groupings. Meta-analyses harness the power of multiple studies to generalize conclusions beyond those of one study. In doing so, meta-analyses may encounter problems from grouping studies together. Here the measures grouped in some domains, such as metabolic variables, were correlated and part of a syndrome. In others, such as the immunologic ones, categorical assortment was more difficult. Antibodies to EBV and HSV were placed in the same category even though they can arise from humoral immunity, cellular immunity, or both. This categorical approach was also used by Herbert and Cohen (1993a, 1993b). Moreover, because of their relationships with each other, IgG responses to specific vaccinations and IgG serum levels were combined. Had we not done this, the number of studies per category would have been greatly limited.

Additional Potential Limitations

Interpretative problems occur in meta-analyses in response to measurement error and inadequate study designs. Here we consider three such problems that are relevant to the current meta-analysis. These include the validity of the health measures used across studies, selection biases, and problems of confounding and reverse causality.

Validity of measures. This article assumes that stressors negatively affect physiological risk, which in turn increases illness risks. Although there are many instances in which such pathways are well known and accepted (Chrousos & Gold, 1992), there are others in which the connections have less empirical support. Clearly, stressors increase stress hormones, which increase glucose and blood pressure. Cholesterol and hypertension increase CHD risk, and high glucose and obesity increase risk for Type II diabetes. Also, wound healing and antibodies to vaccinations and to EBV/HSV each have strong links with health outcomes. In contrast, associations between illnesses with resting plasma IgG levels and lymphocyte proliferation may not be as strong in persons who are not already immunocompromised. Despite such variations, most measures in this review represent attempts by caregiver researchers to use physiological measures that have predictive and concurrent validity (see Table 1). Indeed, in the past 15 years the immunologic measures used have been shown to be more responsive to stressors and clinically relevant. If we had focused only on the small number of immunologic measures currently thought to be important, this review would have been limited and biased. Yet even with these caveats, the current results for antibodies are still consistent with the stress, depression, and immunity meta-analyses of Herbert and Cohen (1993a, 1993b).

Selection bias. All reports in this meta-analysis were based on observations and not experiments, and this may have obscured results. Premorbid differences between caregivers and noncaregivers could have caused the observed point-biserial correlations to be different from those that would have been obtained from randomized studies. Moreover, none of these studies examined individuals before they became caregivers. As such, prior to caregiving, caregivers may have had greater distress and poorer health habits than noncaregivers. Without random assignment of caregivers and noncaregivers, characteristics that occur prior to caregiving and that are known to covary within couples may influence differences in the observed health of caregivers versus noncaregivers. Such correlations can occur because of *assortative mating*—the tendency for individuals to marry persons similar to themselves (Buss, 1984)—and mutual influences on each other's behavior (Vogel & Motulsky, 1986). High within-couple correlations have been found for diet, alcohol consumption, caffeine, tobacco, and medications (Davis, Murphy, Neuhaus, Gee, & Quiroga, 2000; Demers, Bisson, & Palluy, 1999), and Buss (1983) has observed within-couple correlations of .30 for weight, .43 for smoking, and .43 for drinking. These results are important because health habits (Skoog, 1998) and distress (Gale, Braidwood, Winter, & Martyn, 1999; Leonard, 2001) may contribute to the development of dementia and related cognitive disorders. If this is the case, then the same lifestyle that influenced the development of dementia in care recipients may also have influenced the development of other illnesses in caregivers, with genetic predispositions affecting how these shared risk factors manifested themselves differently.

Confounding and reverse causation. To control for differences in caregivers and noncaregivers from unknown confounders, the noncaregivers in this meta-analysis were group matched to caregivers on sex and age. However, it is impossible to match on all variables, and biases can occur if important variables are ignored. Income is one such variable because it is negatively related to health (Kaplan, 1992). In some studies, caregivers and

[6] Draper, Poulos, Cole, Poulos, and Ehrlich (1992) and Reese, Gross, Smalley, and Messer (1994) found no difference in distress between AD and stroke caregivers. Hooker et al. (1998) found that AD caregivers had worse mental health than Parkinson's caregivers, but AD caregivers had better physical health than Parkinson's caregivers, after mental health and personality were controlled.

noncaregivers and male caregivers and male noncaregivers did not differ in income (Vitaliano et al., 2002), but this may not have been true in all studies. Persons who become caregivers may have lower incomes than persons eligible for but who opt out of caregiving. Men may take on caregiving only when they do not have financial resources or a daughter or sister to help them (Kramer, 1997). It is important that income be controlled when comparing the health of male caregivers with male noncaregivers.

In addition to their possible confounding nature, the studies in this meta-analysis are also limited by their cross-sectional design. That is, they do not allow one to determine whether illnesses preceded caregiving or vice versa. To address this concern, some caregiver studies have used prospective designs, in which caregivers and noncaregivers were examined only if they were free of a predicted outcome. Shaw et al. (1997) followed spousal caregivers of AD patients and spouses of noncaregivers over 1–6 years, depending on the care recipient's life course. Caregivers who provided the most assistance had a greater hazard of reaching at least one objective negative health event relative to other caregivers and noncaregivers. This suggests that caregiver stressors may precede their health problems. Schulz and Beach (1999) followed persons who were caregivers of various types of care recipients. They observed that over an average of 4 years, strained caregivers had a 63% higher death rate than noncaregivers. Finally, Vitaliano et al. (2002) observed that men caring for a spouse with AD had a greater prevalence of heart disease than demographically similar noncaregiver men 27–30 months after study entry. Also, the incident cases of heart disease showed a higher trend in male caregivers than in male noncaregivers. No differences occurred for women. In terms of mechanisms, a latent variable of caregiver status and care recipient deficits in cognitive and functional status explained variance in distress. This, in turn, explained variance in poor health habits, which predicted elevated cardiovascular and metabolic risk 15–18 months later. Such dysregulation predicted new cases of heart disease over 27–30 months. As in Figure 1, health habits are part of a major pathway from stressors to health problems (Fuller-Jonap & Haley, 1995). Indeed, Gallant and Connell (1997) observed that caregiver burden was associated with poorer health habits, such as sedentary behavior, alcohol consumption, and smoking. They also concluded that health habits represent one mechanism by which caregiver stressors influence adverse health. Health habits, however, have not received enough emphasis in caregiver research to be examined meta-analytically.

Advances and Recommendations

Despite the above concerns, this article has a number of advantages. Caregiving allows one to examine a naturalistic chronic stressor that is unambiguously defined by the caregiver's self-identification and the care recipient's cognitive, functional, and affective disabilities. Yet there have been relatively few qualitative reviews of caregiver physical health, and this is the first quantitative review. Although qualitative reviews can be of value, meta-analytic reviews have fixed rules for aggregating point-biserial correlations and providing quantitative summaries of the typical strength of a relationship, its variability, and its significance. Moreover, because point-biserial correlations are continuous, they are more accurate than "vote counts" of significant findings in qualitative reviews (Lipsey & Wilson, 2001). For this reason, the results of this meta-analysis should be useful. However, in addition to quantifying the risk of caregiver health problems relative to noncaregivers, these results also suggest directions for future research—namely, the use of a theoretical model of stress and illness, more informative designs, and additional health measures.

Stress–illness models. Understanding health responses to caregiving can be improved by a greater use of models that consider individual differences (Lazarus & Folkman, 1984). Earlier we presented a model in which illness is not just a function of caregiving, but also of vulnerabilities, resources, and their interactions (Vitaliano et al., 1987). Unfortunately, most caregiver research on physical health has not used guiding stress models. Indeed, we were not able to examine most parts of the proposed model in this meta-analysis because very few studies had included the variables necessary for such analyses. For example, caregiver health research has tended to ignore individual differences that would allow one to examine interactions with caregiving. Variables such as psychiatric history, personality, comorbidities, social supports, and income were not reported in sufficient numbers to allow analyses. Potential cognitive mediators relevant to stress–illness relationships were also not reported in sufficient numbers. These include appraised control, self-concept, expectations, and the caregiver's cognitions about his or her illnesses and those of his or her care recipient. The self-regulation model would be useful here because it views caregivers as active agents in their adherence to treatment regimens for themselves and their care recipients (Leventhal, Nerenz, & Strauss, 1982). To change risky health behaviors and manage their illnesses and those of their care recipients, caregivers must possess accurate information about these illnesses. Caregiver illnesses may also be affected by the self-efficacy (Bandura, 1993) of the caregiver. In fact, self-efficacy may influence the role of sex as a moderator of caregiver illnesses. As noted by M. S. Stroebe (1998), widows have higher levels of perceived efficacy than do widowers in interpersonal activities and social support. A woman's confidence in her ability to manage interpersonal activities and her generally larger social networks may help her to adjust more easily to bereavement than a man.

Finally, some researchers have emphasized the positive aspects of caregiving (C. A. Cohen, Gold, Schulman, & Zucchero, 1994) and have reported more positive changes in self-concept in response to caregiving than negative changes (Aneshensel, Pearlin, Mullan, Zarit, & Whitlatch, 1985). As such, positive appraisals need to be related to illness (Walker, Acock, Bowman, & Li, 1996). In the HIV/AIDS literature, the use of social coping among caregivers has been shown to be associated with greater positive affect and lower levels of physical symptoms (Billings, Folkman, Acree, & Moskowitz, 2000). Moreover, Folkman, Chesney, Collette, Boccellari, & Cooke (1996) have shown that if meaning is derived from the caregiver experience, caregivers can maintain positive morale. One would expect that this would also influence physical health outcomes.

Design. Although the three prospective studies discussed above allowed researchers to infer that caregiving preceded the outcomes studied, they were only prospective for illness or mortality and not for caregiving. Hence, no information about experiences prior to caregiving was available. Only studies that are doubly prospective, in which a cohort is examined before caregiving and before a target illness develops, allow one to examine covariation in caregiver exposure and illness relative to psychosocial, behavioral, and physiological changes. One expects that by studying individuals before caregiving takes place, one can assess

whether self-selection occurs and whether postcaregiving illnesses are influenced by precaregiving as opposed to postcaregiving experiences. Doubly prospective studies can be done by combining caregiver research with ongoing population studies. However, illnesses take time to be detected, and extensive follow-up is necessary. Indeed, even when clinical illness is not evident, more innovative designs can be used to contrast caregivers and noncaregivers under acute and chronic stressors. This is important because relationships between acute stressors and psychological distress are heightened in persons with chronic stress (Norris & Uhl, 1993). Also, the hypothalamic–pituitary–adrenal axis becomes sensitized by chronic stress to yield an amplified response to acute stressors (Hauger, Lorang, Irwin, & Aguilera, 1990). For these reasons, researchers should identify caregivers exposed to stressors that exist in addition to caregiving. Comorbidities may increase caregiver distress and interact with caregiving to exacerbate physiological dysregulation (Vitaliano, Russo, Bailey, Young, & McCann, 1993; Vitaliano, Scanlan, Ochs, et al., 1998; Vitaliano, Scanlan, Siegler, et al., 1998). Such research allows one to study whether caregivers with comorbid illnesses have more disease progression than noncaregivers with such illnesses. To be of concern to society, caregiving does not have to cause illnesses; it only has to contribute to illness progression.

Measurement. Physiological assessments have been primarily laboratory measures. Future research can increase ecological validity by assessing such measures in situ over longer time periods. Home ambulatory blood pressures in caregivers may be greater than clinic and work blood pressures (King, Oka, & Young, 1994), especially in the presence of their care recipients (King & Brassington, 1997). Assessments that include medical records, physical exams, and death certificates are also important. Medical records may provide lab results, date, and nature of diagnosis (or *International Classification of Diseases*, 9th edition, codes; Puckett, 1993), treatment, medications, and prognosis. Quality control checklists document treatment regimen and symptoms to support diagnostic codes and assess the internal consistency of records (Hanken, 1989). Physical exams can uncover problems undetected in medical records (Bates, 1995). In terms of illnesses, those with dramatic sudden onsets or a need for medical attention may be more reliably studied than illnesses without such features (Kasl, 1983). Also, measures should be matched to the temporal courses of the stressors and the illnesses being studied (cf. S. Cohen, Kaplan, & Matthews, 1994). Heart disease can take years to develop, so one must specify pathways through which caregiving is expected to influence its development. Measures that have already been used in caregiver research can also be put to better use. Instead of just counting illnesses, researchers should assess which illnesses are most related to caregiving, as well as the frequencies, dosages, and health implications of medications. One can assess the latter by asking participants to bring their medications to one's lab and having a pharmacologist code them. Results for caregiver health service utilization are also difficult to interpret because one must ensure that caregivers are evaluated separately from care recipients and that one allows for the fact that caregivers may be home bound. A final issue involves the simultaneous use of self-report and physiological assessments.

> Assessments that rely solely on self-reports will lead to a targeting of resources away from some caregivers (e.g., men), who may be unwilling or unable to express their distress. Assessments that incorporate cardiovascular reactivity should be better able to identify caregivers who are truly distressed and in need of help. (Lutzky & Knight, 1994, p. 518)

Conclusions

We searched published and unpublished reports over a 38-year period and found 23 studies that compared physical health indicators in family caregivers of persons with dementia to health indicators in noncaregivers who were generally matched on age and sex. Caregivers had a 23% higher level of stress hormones and a 15% lower level of antibody responses than did noncaregivers. Whereas these observational data do not allow us to infer definitively that caregiving is hazardous to one's health, such potential added risks are noteworthy because they may have clinical implications for millions of caregivers. Although researchers would really like to determine whether caregiving "causes" illnesses, regardless of the causes, the fact that caregiving may influence illness is still important. As the world's population ages, caregivers will play an even greater role in society. Science may develop a "cure" for dementia, but other care recipients will need caregivers. In this regard, the current work should be extended to caregivers of care recipients with other chronic illnesses. Moreover, doubly prospective studies of caregiving should be performed to clarify the causes of such added risk, and subgroups of caregivers, such as those with comorbidities, should be examined. General research on chronic stress and illness suggests that persons with comorbidities may be at higher risk for health problems in response to stressors than persons exposed to chronic stressors who are free of comorbidities. The population of older caregivers with comorbidities is large, yet this group essentially has been ignored in this literature, as have other subgroups defined by individual differences. One hopes that the combination of designs recommended here, which incorporates assessments of individual differences and other health indicators, will target high risk caregivers and be used to develop cost-effective treatments for those who can profit most from interventions. By helping caregivers to maintain their health, such interventions should also help care recipients and society.

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