

Health Consequences of Alzheimer's Caregiving Transitions: Effects of Placement and Bereavement

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Objective: To determine the extent to which the chronic stress of Alzheimer's disease caregiving may be alleviated by placement or death of the Alzheimer's disease patient, we prospectively compared groups of caregivers (CG) who continued to care for their Alzheimer's disease spouse at home, CG who placed their spouses, and CG whose spouses died with similarly aged noncaregiving comparison subjects (control subjects). **Methods:** A sample of 119 CG who had been studied for at least 18 months at 6-month intervals was included in the present analyses (ie, had at least three assessments). Data were gathered on CG mood, blood pressure, and medical symptoms among 38 CG whose spouses were at home at all three visits (home-home-home [HHH]); 28 CG who placed their spouse at follow-up (home-placed-placed [HPP]); 27 CG whose spouses were placed and subsequently died at follow-up (home-placed-deceased [HPD]); and 26 CG whose spouses died at home (home-deceased-deceased [HDD]). Data were compared with 48 noncaregiving control subjects (NC group). **Results:** CG in the HPP, HPD, and HDD groups showed improvement in depressive and physical symptoms compared with HHH and NCs. CG had significantly higher systolic blood pressure at rest than did NCs. Both placement and death of the Alzheimer's disease spouse were associated with higher systolic blood pressure in response to postural challenge in CG experiencing these transitions. **Conclusions:** Despite improvement seen in mood and medical symptoms among CG who place their spouses or experience the spouse's death, there may be longer term physiological alterations, possibly in sympathoadrenalmedullary arousal, that cause the cardiovascular system to continue to respond to acute stressors such as postural challenge more actively for a period of 6 to 12 months after such transitions. **Key words:** Alzheimer's caregiving transitions, health outcomes, bereavement, placement.

AD = Alzheimer's disease; ANCOVA = analysis of covariance; ANOVA = analysis of variance; BP = blood pressure; CDR = Clinical Dementia Rating; CG = caregiver; DBP = diastolic blood pressure; HDD = home-deceased-deceased; HDRS = Hamilton Depression Rating Scale; HHH = home-home-home; HPD = home-placed-deceased; HPP = home-placed-placed; NC = noncaregiving control subjects; NK = natural killer cells; SAM = sympathoadrenalmedullary; SBP = systolic blood pressure.

INTRODUCTION

It is estimated that the prevalence of Alzheimer's disease in the United States could be as high as 4.78 million, a figure that is expected to nearly quadruple over the next 50 years (1). Although AD is clearly not a part of normal aging, it is undoubtedly an age-related

disorder. The incidence of disease is low until the age of 65; after 65 it has been shown to double for every 5 years of age (2). The majority of patients with AD are cared for by a family member. Schulz and O'Brien (3) have estimated that there are between 2.4 and 3.1 million AD caregivers in the United States, a number that is expected to rise sharply as the population ages. In many cases, family caregivers are spouses, who are themselves elderly and at increased risk for medical illness and physical injury.

It is widely accepted that providing care for a relative with AD can be a potent source of chronic stress that can lead to deleterious consequences for both the physical health (4–12) and emotional well-being (13–15) of a subset of caregivers. Dementia caregivers have been shown to have more depressive symptoms than noncaregiving control subjects as well as an increased incidence of clinical depressive disorders (16). It has been estimated that between 33% and 39% of elderly dementia caregivers score at or above the Center for Epidemiologic Studies Depression Scale (CES-D) cut-off, indicating that more than one-third of dementia caregivers are at risk for a depressive disorder (17). Similarly, it has been shown that the proportion of dementia caregivers who report the use of psychotropic medication is nearly double that of noncaregiving control subjects (7, 18).

The relationship between providing care for a loved one and the experience of psychological distress has been shown to be influenced by a number of factors, including perceived pressure from informal care (19), coping style (20), patient depression, psychosis, and

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cognitive impairments (21), as well as relationship to the patient (17). Spouses have consistently been found to be more depressed than other relatives (17), and in some (22–24), but not all (16, 25–28) studies, older age has been associated with increased psychological distress. The potentially negative psychological consequences of caregiving are buffered by a number of factors, including instrumental social support (29) and the caregiver's internal resourcefulness (30).

Not all caregiving experiences are negative. For example, caregivers who endorse spiritual beliefs and a coping style involving positive reappraisal report higher levels of positive affect (31), potentially helping to reduce the risk for depression or other psychological distress.

The effects of caregiving on physical health have received increasing attention (4, 5). Caregivers report poorer perceived physical health (17) and more chronic illnesses than noncaregiving control subjects (10). They have been shown to mount poorer immune responses to viral challenges (11), evidence slower rates of wound healing (12), and are at increased risk for developing mild hypertension (32). Furthermore, a recent prospective study (33) found that the relative risk for all-cause mortality among older spousal caregivers experiencing caregiver strain was 63% higher than that which was seen in noncaregiving control subjects.

It has been proposed that caregiving may impact physical health by producing alterations in the sympathoadrenalmedullary axis (4), which is activated in the presence of a stressor. Short-term activation of this system results in a rise in plasma epinephrine and norepinephrine, which in turn act to speed metabolism, alter immune functioning, and increase heart rate and blood pressure in a transient manner. However, long-term or repeated acute activation of this system, as can occur in the context of caregiving, may lead to alterations in the set point of these systems that promote the development of pathophysiological conditions, such as hypertension. Of course, only a fraction of those caregivers exposed to chronically stressful conditions are likely to go on to develop physical symptoms or syndromes. The factors that are thought to mediate and moderate these relationships are similar to those that influence the psychological response to caregiving, including social support (34) and perceived strain (6). And in a similar vein to what was discussed for CG mental health, it has been shown that spouses report worse physical health than do adult children (35). Older age has also been found to predict worse CG physical health (36). In fact, Applegate et al. (37) have presented evidence to indicate that caregiving and similar life stressors pose greater risk of nega-

tively affecting the physical health of older vs. younger adults by causing further impairment to an aging immune system.

Despite the varied factors that may cause the nature of the caregiving experience to differ from individual to individual, it is evident that providing in-home care for a relative with Alzheimer's disease is an involved and often difficult process. It is further complicated by the inescapable fact that the only plausible end to in-home caregiving involves one of two transitions: death or placement of the relative in a care facility.

Either of these transitions away from in-home care could generate conflicting emotions in the caregiver, ranging from a profound sense of loss to relief and gratitude (38). Thus, the effect of either transition on caregiver health could range from having a negative impact on health due to guilt or grief to producing improvements in health due to relief from role overload and role captivity. To date, very little work has addressed the impact of such transitions on CG well-being. The few studies that have been reported have used differing methodology, and their findings have been mixed.

Bodnar and Kiecolt-Glaser (39) examined both syndromal depression and depressive symptoms in former (bereaved) and current caregivers of parents and spouses with progressive dementia as well as in a group of age-matched noncaregiving control subjects. It was determined that although both current and former caregivers evidenced significantly higher levels of syndromal depression and depressive symptomatology compared with control subjects, there was no difference in any measure of depression between the two kinds of caregivers. This result was obtained despite the fact that the average time since bereavement for the cohort of former caregivers was 19.8 months, leading the authors to conclude that impact of caregiving on psychological health persists long after the objective stressor has remitted.

On the other hand, findings from longitudinal studies have shown that after the death of the demented relative, caregivers experience an increase in mastery (a global sense of control) combined with a decrease in role overload, work, and financial strain, circumstances that ought to promote health improvement (40). They also found that although caregivers who placed their relative did not experience a change in mastery, they did experience significant declines in both role overload and role captivity as well as decreases in family tension and work strain. On the basis of these findings, Skaff et al. (40) have suggested that although placement brings much needed relief to some areas taxed by caregiving demands, it also brings with it a new set of stressors (notably financial burden) that

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may offset its ability to increase mastery, and, by association, improve health. The enhanced mastery after death of the afflicted relative may reflect freeing of the caregiver from some of the additional strains brought on by placement.

Aneshensel et al. (41) found that caregivers who placed their relative experienced a significant decrease in anger from baseline (preplacement) levels compared with caregivers who continued to provide in-home care. On average, caregivers who were bereaved did not experience any change in their level of depression from prebereavement levels in the first bereavement year. However, more detailed analysis revealed that depression and guilt rose abruptly in the first month after bereavement and then declined steadily throughout the year. However, although guilt decreased in a purely linear fashion, depression exhibited a curvilinear decline; thus, at 6 months, levels were somewhat lower than those at the baseline assessment, but by 12 months, depression had once again reached prebereavement levels. In a subset of the larger cohort who were followed for up to 4 years, it was shown that depression significantly decreased to levels below the predeath baseline between the first and second bereavement years and remained reduced through the third year of postbereavement data collection. However, the study did not include a noncaregiving comparison group, so it is not possible to determine whether these “reduced” levels would be elevated in comparison to individuals who never performed the caregiving role.

The effect of transitions in caregiving has also been explored in relation to physiological functioning, specifically, in terms of the robustness of immune activation. Esterling et al. (42) isolated NK cells from blood samples of current and former (bereaved) spousal AD caregivers and noncaregiving control subjects; the cells were then treated with cytokines (recombinant interferon- γ or recombinant interleukin-2) that are known to activate a cytotoxic NK response in healthy individuals. In results that parallel those found by Bodnar and Kiecolt-Glaser (39), the authors found that both current and former caregivers demonstrated significant depression in NK activity compared with noncaregiving control subjects; however, current and former caregivers were indistinguishable from one another in terms of their NK response to cytokine stimulation. Furthermore, the results were obtained despite the fact that a mean of 3 years had elapsed since the cessation of caregiving for the bereaved cohort.

Clearly, the nature and duration of the effects of experiencing a major transition in caregiving are complex and may differ as a result of both individual factors such as level of social support or coping style

and environmental factors such as whether their AD relative was residing at home or in a care facility at the time of death. In addition, the transitions of death and placement seem to affect a wide range of systems, and their effects may differ in terms of their magnitude and/or direction depending on whether emotional, physical, or physiological health outcomes are being assessed.

The present study sought to simultaneously examine the psychological, physical, and physiological effects of placement and/or death of a spouse with Alzheimer's disease. Placement was defined as moving the AD spouse from the home to more protective arrangements such as assisted living communities or other long-term care facilities. We hypothesized that CGs would report fewer depressive and physical symptoms and demonstrate reductions in blood pressure after the death or placement of their spouse.

METHODS

Subjects

This study was conducted in the context of a larger longitudinal investigation of Alzheimer caregiving stress, some aspects of which have been described previously (32, 43, 44). In brief, the parent study recruited a group of 201 spousal CG of Alzheimer's disease relatives into a longitudinal investigation in which the caregivers were assessed every 6 months. For the purposes of this report, we selected the 119 caregivers who had been in the study long enough to have at least three 6-month blocs of observation over a period ranging from 18 to 48 months total. The parent study also evaluated couples of comparable age with the Alzheimer's disease pairs, but neither of whom required care. One of the spouses was selected to serve as a noncaregiving control (NC, $N = 49$ in the original study). A comparison of caregivers who are included in the present report ($N = 119$) with those who were excluded ($N = 82$) revealed that these two samples did not differ in age ($t = 1.64, p > .05$) or degree of dementia ($\chi^2 = 2.9, p > .05$). As might be expected (because a requirement of the study was to be caregiving and enrolled in the study long enough for transitions potentially to occur), participants who were excluded from analyses had been caregiving for a shorter period of time compared with those who were included (mean months of caregiving \pm SE = 50.4 ± 6.0 vs. 104.6 ± 5.9) and had been enrolled in the study for a shorter period of time compared with those who were included (mean months in study 13.1 ± 0.9 vs. 22.4 ± 1.2).

The objective of this study was to determine the medical and psychological correlates of two important transition events: placement of the AD relative and death of the AD relative. For this purpose, we identified caregivers who had the following transition experiences: 1) CG who continued to look after their relative at home throughout the period of observation—this meant that for at least three blocs of observation, the status of caregiving was HHH ($N = 38$); 2) CG who began with home care, then placed during the second observation bloc, with the patient remaining placed throughout the follow-up—the HPP group ($N = 28$); 3) CG who began with home care, then placed, and on a subsequent occasion, the AD spouse died—the HPD group ($N = 27$); 4) CG who began with home care, then at a subsequent 6-month follow-up time, the AD spouse died while in home care, and we then obtained an additional 6-month

follow-up on CG status (ie, approximately 12 months after death of the patient—the HDD group ($N = 26$). Because caregivers occasionally were too distraught to be interviewed at the immediate 6-month follow-up after patient death, the actual follow-up period was 8.7 months (range = 6–12 months) and 7.4 months (range = 6–12 months) in the HDD and HPD groups, respectively. In addition, there were 48 noncaregiving control subjects (NC group) who completed at least three 6-month evaluation blocs.

The demographic characteristics of subjects are shown in Table 1. The typical caregiver was approximately 70 years old at study entry and reported education and highest head of household occupation to place them into the middle to lower-middle class status. The CG were 60% women, and the transition groups did not differ systematically in age, SES, or gender distribution. HHH caregivers reported duration of caregiving of somewhat briefer duration than those whose spouses were subsequently placed or died. Not surprisingly, patients who were subsequently placed or died were also more demented (Table 2). The CG were comparable with NC, with the exception that NC were of slightly higher social position and better educated.

Methods

Subjects were evaluated in their homes every 6 months by trained research staff. Research nurses obtained the medical and blood pressure data, whereas a psychology research assistant gathered psychosocial and demographic data. In the parent study, data were gathered on caregiver medical and psychological symptoms, social supports, coping, as well as changes in the AD spouse's dementia status. For the purposes of this report, we focused on the following observer-rated CG health indicators: depressive symptomatology, medical symptoms, and blood pressure as an indicator of cardiovascular response to possible sympathoadrenalmedullary activation related to caregiving stress.

Stage of dementia. The CDR scale of Hughes et al. (45) was used to classify AD patients as questionable, mildly demented, moderately demented, or severely demented. The CDR was assigned by a research nurse who obtained information from the caregiver concerning patient functioning in six domains: memory, orientation, judgment/problem solving, community affairs, home/hobbies, and personal care.

Length of time caregiving. Caregivers were asked how long they had been in that role, defined as time since diagnosis.

Depressive symptoms. The presence of symptoms associated with depression was assessed by the observer-administered 17-item HDRS (46).

Medical symptoms. The research nurse systematically queried the subject regarding presence in the past 6 months of various

physical symptoms, using a review of systems guided questionnaire. This questionnaire probes 16 areas such as “Have you often had bad headaches?” or “Have you had repeated pain (or pressure or tight feeling) in your chest?” If the participant responds affirmatively, she/he is queried about details. For example, in regard to chest pain, examples of follow-up questions are “Did the pain force you to stop walking?” or “Did the pain last more than 10 minutes?” This method has been described previously (44, 47). Based on this inventory, it is possible to group symptoms as “serious” and “nonserious.” The distinction was based on physician judgments as to the likelihood that a particular symptom connoted a medical condition that either ought to be evaluated further or ought to be treated. For example, onset of cough with productive sputum, episode of fever, or burning on urination would be classed as serious, whereas minor back pain and stuffy nose or itchy eyes would be considered nonserious. In this study we computed total serious and nonserious medical symptom scores.

Blood pressure. Previously, we observed that some CG had greater BP rise from supine to standing than NC (48), suggesting possible sympathoadrenalmedullary activation. BP data were gathered in subjects' homes using a semiautomated sphygmomanometer (Critikon Dynamap 8100, Critikon, Largo, FL). Subjects relaxed supine for 15 minutes before resting BP was obtained. The standing BP was taken after 2 minutes of standing.

Selection of time blocs for analysis. Because there was no way of predicting which CG would end up in which transition group, by necessity the classification of subjects occurred after the fact. At each 6-month follow-up, we determined whether the patient-spouse was placed or had died in the preceding 6-month period. If either event occurred, then the time period during which this happened was one of the blocs chosen for analysis. In some instances, the CG was not available for evaluation within the first 6 months of the event. In that case, the next 6-month time bloc was used for analysis. Therefore, the transition bloc time frame spanned 6 to 12 months after the event. Additionally, the 6-month time bloc immediately preceding the bloc that contained the transition event and the time bloc immediately after the transition bloc were selected for analysis. In the case of the HHH CG and NC comparison group, we selected contiguous time blocs from a larger set to be as comparable as possible to those from the transitioning groups in terms of length of time the subjects had been in the study.

Statistical Analyses

We performed repeated-measures ANOVA with subject group (transition classification) as the between-subjects factor and the three times as the within-subjects factor. The dependent variables were total HDRS as a measure of depressive symptoms, total serious

TABLE 1. Characteristics of Caregivers by Transition Group

| Group | Age | Gender (Male %) | Education | SES ^a | Months Caregiving ^b |
|---------------------------|------------|-----------------|------------|------------------|--------------------------------|
| Home—home—home CG | 69.8 ± 6.7 | 43.8 | 14.8 ± 3.2 | 37.2 ± 17.9 | 81.2 ± 11.7 |
| Home—placed—placed CG | 70.2 ± 7.2 | 33.3 | 13.6 ± 3.4 | 36.7 ± 15.0 | 101.1 ± 11.2 |
| Home—placed—deceased CG | 69.9 ± 6.3 | 24.2 | 14.0 ± 2.2 | 40.7 ± 18.0 | 113.6 ± 10.8 |
| Home—deceased—deceased CG | 72.7 ± 8.2 | 38.2 | 14.3 ± 2.5 | 37.2 ± 15.4 | 133.2 ± 11.1 |
| Home—home—home CTRL | 69.5 ± 7.4 | 51.0 | 15.7 ± 2.8 | 28.5 ± 16.5 | N/A |

ANOVA—Age: $F = 1.2$, $P > .05$; Gender: $\chi^2 = 6.9$, $P > .05$; Education: $F = 3.5$, $P = .01$; SES: $F = 3.2$, $P = .02$; Months Caregiving: $F = 2.8$, $P < .05$

^a SES = socioeconomic status; Hollingshead raw score (55).

^b Months caregiving calculated from time of patient diagnosis to initial home visit.

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TABLE 2. Clinical Dementia Ratings of Patients by Transition Group

| Group | Healthy (%) | Questionable (%) | Mild (%) | Moderate (%) | Severe (%) |
|---------------------------|-------------|------------------|----------|--------------|------------|
| Home—home—home CG | | 17 | 48 | 15 | 20 |
| Home—placed—placed CG | | 3 | 25 | 42 | 30 |
| Home—placed—deceased CG | | | 10 | 35 | 55 |
| Home—deceased—deceased CG | | | | 41 | 59 |
| Home—home—home CTRL | 100 | | | | |

and nonserious medical symptoms, and supine and standing systolic and diastolic blood pressures. Group by time interactions were of particular interest as indicators of transition effects on the dependent health measures. The analyses were repeated after entering covariates that might have contributed to the results. These included the spouse's CDR and length of caregiving at entry to the study.

RESULTS

Depressive Symptoms

Although depression scores were generally low and no subject was clinically depressed, repeated-measures ANOVA (5 groups, 3 time blocs, HDRS total score dependent) evidenced a significant group by time interaction ($F = 2.3, p = .02$). Inspection of HDRS scores for each group at each time period revealed that whereas the HHH CG group and the NC comparison subjects had relatively stable depression scores over the three time periods, CG in the three groups that experienced transitions all had significant improvement in scores 6 to 12 months after placement or death of their spouse. These changes are presented in Figure 1.

For the HPP caregivers who placed by time 2 and maintained placement at time 3, there was improve-

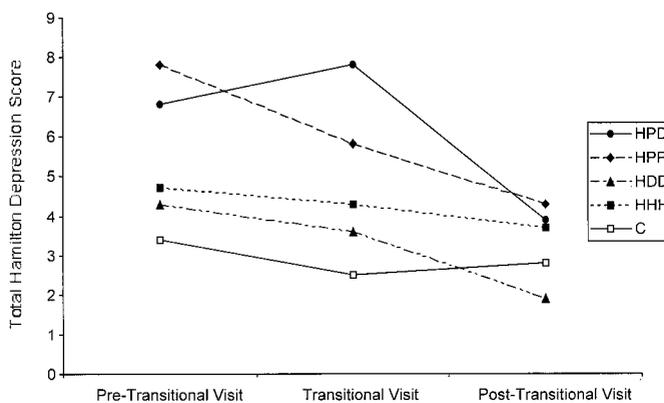


Fig. 1. Mean Hamilton depression scores at pretransitional, transitional, and posttransitional visits for CG whose spouses were at home at all three visits (HHH), CG who placed their patient at follow-up (HPP), CG who placed spouses with subsequent death of the spouse at follow-up (HPC), CG whose spouse died at home (HDD), and noncaregiving control subjects (C).

ment within 6 months (time 2 HDRS declined from 7.8–5.8) and further improvement approximately 12 months after placement (HDRS = 4.3). In the HPP CG, who placed by time 2, with death of their spouse by time 3, the HDRS increased from 6.8 at time 1 to 7.9 at time 2 but declined substantially to 3.9 by time 3. For HDD CG, the death occurred while the patient was still at home during time 2. HDRS was unchanged statistically between time 1 (4.3) and time 2 (3.6). However, by approximately 12 months after death of their spouse, the depressive score average for this group improved to 1.9.

There were also significant main effects for group ($F = 3.9, p = .01$) and time ($F = 17.2, p = .001$). The former reflects the generally lower depression symptom scores in the NC group compared with all CG groups. The time effect seems to represent the marked improvements in the three transition groups, plus a slight tendency for HHH CG and the NC to report fewer depressive symptoms over time (Figure 1).

Depressive Symptom Subtypes

To determine whether observed changes in depressive symptoms were being driven primarily by either biologic symptoms (eg, improved sleep) or emotional changes, we computed total “vegetative” and “affective” scores by summing items that fit best into physical vs. emotional domains. Repeated-measures ANOVA, modeled as above, revealed significant time by group interactions for the affective component of Hamilton total score (affective: $F = 3.28, p = .03$), but not for the vegetative component (vegetative: $F = 1.53, p = .20$).

Effects of Covariates (CDR and Caregiving Time)

Separate ANCOVAs were performed with the two depression scores (vegetative and affective). Neither CDR of the patients at first evaluation nor length of caregiving were significant covariates. However, the ANCOVAs revealed significant group by time interactions for both dependent variables (vegetative: $F = 3.60, p = .009$; affective: $F = 3.02, p = .016$).

Medical Symptoms

Two repeated-measures ANOVAs were conducted: one with serious symptoms and the second with non-serious symptoms. For the analysis of serious medical symptoms there was again a significant group by time interaction ($F = 2.2, p = .03$). The results are presented in Figure 2. In this case, two of the three CG transition groups contribute to this result. The HPP group reported fewer serious symptoms at time 2 (in the immediate period after placement), and this was sustained at time 3. The group experiencing placement during time 2 and bereavement during time 3 (HPD) showed little change in these medical symptoms at time 2 or at time 3. The average serious medical symptom score for the HDD group was unchanged at time 2 (immediately after death of spouse), but dropped about 30% by time 3 (approximately 12 months after death). Also possibly contributing to the interaction were the scores in the HHH group. For reasons that are unclear, the serious medical scores of that group declined between time 2 and time 3. With CDR and length of caregiving entered into an ANCOVA, neither covariate was significant, but the interaction of group by time also became nonsignificant, presumably reflecting attendant loss of power. For the nonserious medical symptoms, there was no significant group by time interaction ($F = 1.3, p = .23$), indicating that milder medical symptoms were not changing in relation to transition experiences.

Blood Pressure

Resting (supine) BP. Repeated-measures ANOVAs were conducted separately SBP and DBP at rest. There

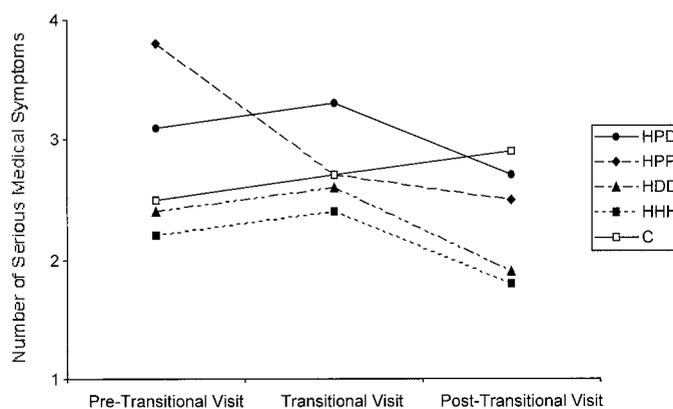


Fig. 2. Mean number of severe medical symptoms at pretransitional, transitional, and posttransitional visits for CG whose spouses were at home at all three visits (HHH), CG who placed their patient at follow-up (HPP), CG who placed spouses with subsequent death of the spouse at follow-up (HPD), CG whose spouse died at home (HDD), and noncaregiving control subjects (C).

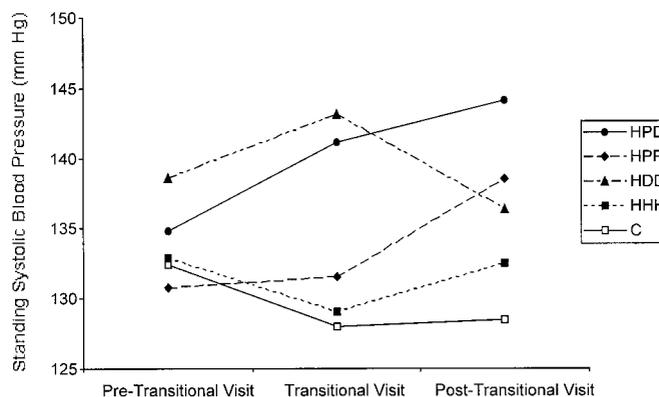


Fig. 3. Mean standing systolic blood pressure at pretransitional, transitional, and posttransitional visits for CG whose spouses were at home at all three visits (HHH), CG who placed their patient at follow-up (HPP), CG who placed spouses with subsequent death of the spouse at follow-up (HPD), CG whose spouse died at home (HDD), and noncaregiving control subjects (C).

was a significant group main effect for resting SBP, but no significant time effect or group by time interaction. The group effect reflects the tendency for SBP to be higher in all CG (131.7 (18.5)) vs. NC (123.4 (14.3)). For resting DBP there were no significant main effects or interaction.

Blood pressure after postural challenge. Repeated-measures ANOVA for standing SBP revealed no significant main effects, but there was a significant group by time interaction ($F = 2.4, p = .02$). Inspecting the standing SBP averages for each group at each time period, we noted that the CG groups experiencing transitions seemed to be responsible for the interaction (Figure 3). Both placement and spousal death seemed to be associated with standing SBP rise. Thus, SBP among HPD is higher at time 2, and remains so at time 3; and in the HDD group, the standing SBP rises in the period immediately after death of spouse, but tends to return to prebereavement level approximately 12 months after death. When covariates were entered, the group by time interaction for SBP reactivity became a trend ($F = 2.39, p = .057$). Months of caregiving was significantly related to SBP reactivity ($F = 3.11, p = .05$), but CDR was not. In regard to DBP after postural challenge, there were no significant main effects nor significant interaction. In summary, there is a suggestion that cardiovascular response to physiological stress (postural challenge) may be affected by placement and bereavement transition events. In this instance, length of caregiving also independently predicted higher SBP after postural challenge, consistent with our previous report (32).

DISCUSSION

Caregiving for a relative with AD can be stressful in many ways and has been documented extensively in previous research (17). Two critical transitions faced by many caregivers are placement and death of the AD relative. Although both of these issues have received attention in prior research, the present study may be the first to examine the possible health effects of each of these transitions, as well as the combination of the two, in a prospective design. In our study, caregivers were all spouses who were providing care at home when the observations began. Therefore, we had baseline data on these subjects against which we could compare information gathered at two follow-up periods—periods during which some caregivers placed, some experienced bereavement, and others went through both. Prospectively gathered data were also available for caregivers who continued to care at home, as well as on a control group of elders who were married, but whose spouses did not have Alzheimer's disease and did not require any other form of caregiving.

We chose to examine the associations of transitions to three indicators of caregiver health: mood, medical symptoms, and blood pressure. The latter included response of BP to postural challenge as a possible window into cardiovascular reactivity that might be influenced by stress-related changes in sympathoadrenal-medullary tone. In part, the choice of these measures was influenced by our desire to have some data from the psychological, physical, and physiological domains. We were also cognizant of prior research suggesting that depression accompanies caregiving (13–15) and that some caregivers experience more medical illnesses (7–10). Prior work, including our own (32), also indicated that caregivers tend to develop elevated blood pressure. Thus, it seemed important to determine whether these symptoms and signs improved with placement or worsened with bereavement and to plot the time course of such changes. To the extent possible, we also selected measures that were observer rated to avoid possible minimization and amplification effects that can occur in purely self-report measures.

Concerning symptoms of depression, we noted that CG, as a group, had significantly higher scores on the Hamilton Depression Rating Scale than age- and gender-comparable NC control subjects. This confirms previous reports on worse mood in CG, although we should emphasize that although CG reported more depressive symptoms than control subjects, the HDRS average remained well below that seen in clinically depressed persons. Indeed, none of our CG exceeded

an HDRS score of 17, typically considered the cutoff for major depression.

CG who placed their spouse had a decline in depressive symptoms in the 6-month period during which placement occurred, and these symptoms improved further within 12 months of placement. Similarly, among the CG whose spouse died while care was being provided at home, there was no significant change in depressive symptoms at 6 months, but substantial improvement by 12 months. The CG who placed with subsequent death of their spouse also had improvement in depression at 12 months.

These data suggest that both placement and death of the demented relative can have beneficial effects on the mood of the CG, but that this effect can take 12 months to become evident. In both instances, it may be the case that relief from the chronic worry and emotional and physical demands of caregiving result in improved psychological status of the caregiver and that this relief outweighs whatever increase in depression might be expected from a sense of guilt over placement or loss after death. Such improvements in mood may also reflect the fact that many caregivers have gradually worked through their sense of loss of the loved one during the lengthy caregiving period and, in fact, have detached themselves psychologically from their spouse even before placement. Placement and death could then be seen as a natural process of psychological accommodation to loss of the spouse first as a psychological entity and finally in a physical sense.

Changes in serious medical symptoms largely paralleled those in depressive symptoms. These medical symptom observations, by reinforcing the findings in regard to depressive symptoms, add credence to the notion that both placement and death of the AD spouse are accompanied, in the longer term, by health benefits to the caregiver. It is important to note that this pattern of change was seen in the symptoms termed serious from a medical vantage point. No such changes were observed in the more common nonserious symptoms. This suggests that changes in these medical symptoms are not explained solely by increased or decreased tendency to complain that can accompany mood changes. Rather, because changes were seen principally in more severe medical symptoms, it could be that there is actually some lessening of biological vulnerability to illness in the CG after placement and death of the Alzheimer spouse. The mechanisms underlying such a reduction in vulnerability are speculative at this point, but might include favorable modifications in cellular immunity (49), perhaps mediated by decreased arousal of the hypothalamic-pituitary-adrenal axis, or of the SAM system (4).

The possible involvement of the SAM system in various physiological and physical changes that may accompany caregiving is suggested by our findings on blood pressures in the CG. Although blood pressures were generally not in the hypertensive range, CG had significantly higher systolic BP at rest than did non-caregiving control subjects, confirming our previous observations (32). Of greater interest from a theoretical perspective was the current observation that the short-term (6 months) correlate of placement was a higher systolic blood pressure in response to postural challenge; a similar pattern was seen after death of spouse. The BP data diverge from the patterns seen for mood and medical symptoms and indicate that despite improvement in those symptom variables, there may be a longer term physiological alteration, probably in sympathoadrenalmedullary arousal, that causes the cardiovascular system to continue to respond with heightened systolic BP response to a stressor for 12 months or more after bereavement or placement. In effect, if our observations are correct, there may be a lengthy period of physiological readjustment after placement or death of the AD spouse during which new stressors might yet place a CG at risk for cardiovascular illness.

Although several other studies have examined the effects of spousal placement or death, the current research may be novel in that our long-term prospective design allowed us to observe some CG going through both major transitions in a sequential manner. In this way, the effects on mood, medical symptoms, and blood pressure response to postural challenge could be mapped in the same person. Another strength of the current study was the selective inclusion of a homogenous subset of particularly at-risk caregivers, that is, elderly spousal caregivers of AD patients. Caregiver burden has been shown to be greater in spouses than in adult children in both stroke and dementia caregivers (50, 51). Also, as mentioned earlier, spouses and older caregivers have been shown to have more psychological distress (17) and poorer physical health (17, 36, 37) than nonspousal family members and younger caregivers, respectively. In addition, several studies have found that CG of persons with AD and other progressive dementias tend to suffer worse mental and physical health consequences than do caregivers of relatives with cancer, Parkinson's disease, and other nondementing disorders (52–54). In fact, Ory et al. (54) have demonstrated that in addition to being in poorer mental and physical health, caregivers whose relatives have dementia spend more time providing care, have more employment complications, have fewer hours to spend in leisure activities or with other family members, and experience greater caregiver strain than do

caregivers whose relatives are nondementia. Taken together, these findings indicate that as a group, older spousal CG of AD patients may be especially vulnerable to the deleterious effects of caregiving and may be a good target group for interventions.

However, there are also clear limitations to the present study. Once the 119 CG were classified into four transition patterns, the sample sizes became as small as $N = 26$ in the HDD group. This means that our observations must be considered preliminary. The modest subject numbers also limited our ability to model a number of variables in our analyses, some of which might have shed more light on the processes involved. Although two obvious covariates—severity of spousal dementia and duration of caregiving—seemed not to exert a significant influence on our results, other factors such as type and suddenness of death, the family's social support and financial status, availability and use of formal resources, the preexisting health of the CG, the caregiver's specific ways of coping with the dementia relative, and the caregiving challenge generally were not considered. Future research with larger samples could advance our understanding of these transitions by modeling such variables.

In addition, once studies progress to confirming associations along the lines reported here, it will be important for future research to be designed in a manner that begins to address mechanisms that underlie the symptoms and phenomena that are observed. For example, if cardiovascular response to acute stressors indeed distinguishes one group of caregivers from another, is there evidence that increased SAM tone is involved? Measures of circulating catecholamines and neuropeptide Y might provide a window into this question. Similarly, studies involving heart rate and blood pressure variability could provide evidence for altered autonomic modulation (eg, parasympathetic withdrawal) in highly stressed caregivers.

Ultimately, larger scale studies along these lines can help identify CG who may be at particular risk for worse medical outcomes. For example, it is unlikely that all CG who place or become bereaved will experience negative consequences. The challenge will be to characterize the vulnerable CG who, by virtue of medical or psychological predisposition may be predicted to experience greater difficulty in a particular context. In addition, caregiving must be examined in the context of the life course of both the patient and the caregiver. This study investigated a group of CG who were fairly homogenous in terms of their stage of life and relationship to the AD patient. Therefore, our conclusions may not generalize to other groups of CG, for example, middle-aged adult children who may play

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multiple caregiving roles (children as well as parents). Transitions such as placement and bereavement also may have different meaning, and therefore a different health impact when the family member in question is a parent instead of a spouse. Certain health consequences of providing care may be more pronounced in an elderly population, who by virtue of their age are at increased risk for disorders such as depression and cardiovascular disease. Previously identified predictors of well-being, such as sociodemographic characteristics, the nature of the caregiving situation, and social and personality factors, may also influence health outcome differently as a function of the caregiver's age, stage of life, or relationship to the patient. Similarly, interventions may need to be tailored to fit the particular needs of different subgroups of caregivers.

In conclusion, previous studies of the effects of placement and bereavement on caregivers have focused primarily on either psychological or physiological outcomes. This study provides evidence that although caregivers may find psychological relief, altered physiological stress responses may persist for longer periods. The challenge of future research will be to define who the vulnerable caregiver is and to determine whether interventions designed to reduce stress responses—eg, respite or coping skills training—can improve both the psychological and physiological health of such caregivers.

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