A Longitudinal Study of the Relationship Between Levels of Depression Among Persons With Alzheimer’s Disease and Levels of Depression Among Their Family Caregivers

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The purpose of this study was to examine the effects, over time, of depressive symptoms in persons with Alzheimer’s disease on depression in their family caregivers. In a sample of 353 patients and caregivers, multilevel longitudinal analysis was used to accommodate an observational design in which the number of observation points and the intervals between points varied across caregivers. The rate of change (increase) in caregiver depression was predicted by the rate of change (increase) in patient depressive symptoms and by increase in patient dependency in instrumental activities of daily living (ADLs). Acceleration of the increase in caregiver depression was predicted by acceleration in patient dependency in instrumental and basic ADLs but not by acceleration in patient depressive symptoms. These findings indicate the importance of measuring the rate and acceleration of change in patient characteristics in order to understand caregiver depression. They also support early interventions for caregivers.

It is well documented that family caregivers of persons with dementia have significantly more depressive symptoms than age- and gender-matched noncaregivers (Gallagher, Rose, Rivera, Lovett, & Thompson, 1989; Schulz, Visintainer, & Williamson, 1990). Furthermore, caregivers of persons with dementia report more emotional strain and depressive symptoms than caregivers of persons who are not demented (Hooker, Monahan, Bowman, Frazier, & Shifren, 1998; Ory, Hoffman, Yee, Tennstedt, & Schulz, 1999). Prevalence rates for depressive symptoms among caregivers of persons with dementia are reported to range from 28% to 55% (Schulz, O’Brien, Bookwala, & Fleissner, 1995). The characteristic of the person with dementia most consistently found to be associated with caregiver depression is the extent to which the person exhibits problem behaviors (Schulz et al., 1995). Problem behaviors include a wide range of symptoms, including mood disorders (such as depression and anxiety), activity disturbances (such as wandering and restlessness), disruptive and demanding behaviors (such as physical and verbal aggression), and psychotic symptoms (such as paranoid delusions). The purpose of this study was to examine one type of problem behavior in persons with dementia, depressive symptoms, and to determine the effect over time, using multilevel analysis, of change in patient depressive symptoms on change in caregiver depression. To account for general decline in patient functioning and its contribution to caregiver depression, we added as control variables patient dependency in basic and instrumental activities of daily living (BADLs and IADLs, respectively). Additional control variables included duration of illness, caregiver relationship to the patient (spouse vs nonspouse), and caregiver gender and self-reported health.

Between 40% and 50% of persons with Alzheimer’s disease have depressive symptoms, whereas the proportion with actual depressive disorders ranges between 10% and 20% (Alexopoulos & Abrams, 1991; Katz, 1998; Wragg & Jeste, 1989). However, few investigators have examined the effect of depressive symptoms in persons with dementia on depression in their caregivers. Drinka, Smith, and Drinka (1987) reported that severity of patient depression was positively associated with severity of caregiver depression, but severity of patient dementia and dependency in ADLs were not. Their sample (N = 127), however, was from a geriatric clinic where the patients were of advanced age (62% were older than 80), had multiple medical problems, were highly depressed (69% met the criteria for major depression of the third edition of the Diagnostic and Statistical Manual of Mental Disorders; American Psychiatric Association, 1980), and were not all demented (73% met criteria for dementia). Also, their caregivers had an atypically high prevalence (83%) of major depression, all of which limits the generalizability of their findings.

Hadjistavropoulos, Taylor, Tuokko, and Beattie (1994), in a sample (N = 136) from an outpatient diagnostic clinic where 77% of patients met criteria for dementia, found that patient self-report of depressive symptoms was weakly associated with caregiver burden, but caregiver report of patient dysphoria was strongly associated with caregiver burden. They did not measure caregiver depression. Caregiver burden, however, has been shown to be positively associated with caregiver depression (Pruchno, Kleban, Michaels, & Dempsey, 1990; Stuckey, Neundorfer, & Smyth, 1996). The weaker correlation may be due to patient underreporting of depressive symptoms; patient underreporting when...
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compared with reports of caregivers and clinicians is well documented (Burke et al., 1998; Mackenzie, Robiner, & Knopman, 1989; Teri & Wagner, 1991). The only other patient deficit that was significantly correlated with caregiver burden was caregiver perception of greater dependency in IADLs.

Brodaty and Luscombe (1998) examined the association between caregiver psychological morbidity and patient depression in 193 patients diagnosed with dementia at a memory disorder clinic and their caregivers. Caregiver psychological morbidity (including depressive symptoms) was significantly associated with patient depression, both clinician rated and patient self-rated. Caregiver psychological morbidity was also significantly higher for women, spouses, and caregivers living with the patient, as well as for caregivers of patients with demanding problem behaviors, higher severity of impairment in IADLs, and greater cognitive impairment. A logistic regression analysis identified patient depression (clinician rated, but not patient self-rated) and demanding problem behaviors as being independently and significantly associated with caregiver psychological morbidity. In contrast, results from three studies (Cummings, Ross, Absher, Gornbein, & Hadjistavropoulos, 1994; Moye, Robiner, & Mackenzie, 1993; Ott & Fogel, 1992) showed no correlations between patient depression and caregiver depression. All samples, however, were small (Ns = 33, 31, and 50, respectively).

Conclusions from these studies of the relationship between patient depressive symptoms and caregiver depression are limited because of several factors. Samples from some studies included patients not diagnosed with dementia (Drinka et al., 1987; Hadjistavropoulos et al., 1994), and some sample sizes might have been too small to detect effects (Cummings et al., 1995; Moye et al., 1993; Ott & Fogel, 1992). Also, the measures of patient depression and caregiver depression, and their sensitivities, differed among studies. Only three studies (Brodaty & Luscombe, 1998; Drinka et al., 1987; Hadjistavropoulos et al., 1994) controlled for other patient characteristics, such as dementia severity and dependency in ADLs, and only Brodaty and Luscombe controlled for caregiver demographic characteristics, such as gender, relationship to the patient, and coresidence with the patient. Finally, all studies were cross sectional. Thus, this study sought to examine the relationship between patient depression and caregiver depression among well-characterized dementia patients, while controlling for dependency in ADLs and duration of illness, as well as relationship (spouse vs nonspouse), caregiver gender, and self-rated health. Caregiver self-rated health was added because of its strong reciprocal relationship with depressive symptoms (Aneshensel, Frerichs, & Huba, 1984). Further, in this study, the relationship between patient depression and caregiver depression was examined over time to answer (a) to what extent does patient depression change? (b) to what extent does caregiver depression change? and (c) to what extent do patient depression and caregiver depression vary together?

Most, but not all, cross-sectional studies of depressive symptoms in dementia patients have indicated a decrease in the frequency of depression in patients with more advanced dementia, but findings have depended on assessment criteria (Katz, 1998; Payne et al., 1998). Findings from the few longitudinal studies that tracked patient depression and dementia beyond 1 year showed little progressive worsening of patient depression (Devanand et al., 1997; Marin et al., 1997).

From longitudinal studies of depression in caregivers of community-residing persons with dementia (Alspaugh, Stephen, Townsend, Zarit, & Greene, 1999; Aneshensel, Pearlin, Mullan, Zarit, & Whitlatch, 1995; Goode, Haley, Roth, & Ford, 1998; Pruchno et al., 1990; Schulz & Williamson, 1991; Vitaliano, Russo, Young, Teri, & Maiuro, 1991), the general picture is one of caregivers as a group showing stability in depression. However, subsets of caregivers either decrease or increase in depression. For example, Schulz and colleagues reported that, over 2 years, the majority of caregivers (59%) had little change in depression, with three quarters of these stable individuals consistently asymptomatic (below the threshold for risk for clinical depression), whereas one fourth (13.7% of the whole sample) were consistently symptomatic. The remaining caregivers (41%) exhibited fluctuating patterns of depression, with an increase in depression over time. Cross-sectional multivariate analyses at three time points revealed significant positive relationships between caregiver depression and patient behavior problems, but not dependency in either BADLs or IADLs.

Aneshensel and associates (1995) reported the most detailed analysis of the impact of both patient and caregiver characteristics, and the change in these characteristics, on caregiver depression. Examining the caregiving career over 3 years duration, they concluded, “It is evident that the patient’s impairment, its behavioral manifestations, and the resulting dependences are a core catalyst in the stress-proliferation process, especially the rate of decline exhibited as time progresses” (p. 148). Although they did not examine patient depressive symptoms per se, they emphasized that it is not so much the level of patient impairment but the rate of decline that is important to caregivers’ feelings of depression. This supports the emphasis in our study on analysis of rate of change in patient characteristics for their impact on rate of change in caregiver depression.

To examine change in patient characteristics in order to understand change in caregiver depression, we used multilevel analysis for statistical analysis in this study. This technique is well suited to examination of the extent to which patients change in their illness characteristics, the extent to which caregivers change in depression over time, and the extent to which these two processes vary. It can account for different starting points, different duration, different rates of change, and multiple correlates of status and change, which themselves might be changing. The hypothesis for the present study was that as patient depressive symptoms increase, caregiver depression increases, regardless of duration of illness and patient dependency in ADLs, caregiver gender, relationship, and self-reported health.

METHODS

Sample

Participants in this study were 353 persons with dementia who were enrolled in the University Hospitals of Cleveland/
Case Western Reserve University Alzheimer’s Disease Research Center (ADRC) and their family caregivers. Caregiver and patient depression measures were collected from October 1992 through March 1999. All patients were living in the community throughout the study. Using criteria of the National Institute of Neurological and Communicative Disorders and the Stroke/Alzheimer’s Disease and Related Disorders Association (McKhann et al., 1984), 63% of patients were diagnosed with probable Alzheimer’s disease (AD), 31% were diagnosed with possible AD, and 6% were diagnosed with other dementias. Among those diagnosed with possible AD, 37% were diagnosed with possible AD with depression. Duration of illness ranged from 1 year to 11 years, with a mean of 4 years. For dementia severity at the beginning of data collection, as measured with the Clinical Dementia Rating scale (Hughes, Berg, Danziger, Coben, & Martin, 1982), 4% were rated 0.5 (uncertain dementia, all of whom were rated as 1 at the next annual evaluation), 61% were rated 1 (mild dementia), 25% were rated 2 (moderate dementia), 10% were rated 3 (severe dementia), and fewer than 1% were rated 4 (profound dementia).

The patients were mostly female (53%), with a mean age of 73 years (range = 50 to 95 years) at the beginning of data collection. Eighty-seven percent of the patients lived with their caregivers at the beginning of data collection, and 88% were living with their caregivers at the last data collection point. African Americans made up 10% of the sample. Caregivers were mostly female (67%), with a mean age of 64 years (range = 31 to 86 years). The majority were spouses (43% wives and 28% husbands), and 18% were daughters, 5% were sons, and the rest were other relatives.

The design was to collect data on patients at their entry and subsequent annual ADRC visits. At these visits, caregivers were given self-administered questionnaires to complete and mail back. The response rate for caregivers was consistently 90%; all questionnaires were returned within 90 days of the patient’s visit; and, for each patient, the caregiver was the same person throughout this study. Although the basic design called for the assessment of patient and caregiver characteristics on an annual basis for as long as the patient remained in the community, a subset of caregivers (46%) were enrolled in a separate study of caregiver depression and were quarterly asked to complete the questionnaires and answer questions about patients’ ADLs and behavioral symptoms. This supplementary study resulted in up to four additional measurements per caregiver and patient on these variables.

Our data collection design resulted in a variable number of data points and variable time intervals between data collections. For 40% of all caregivers, there was 1 data point at which the outcome variable, caregiver depression, was measured; for the rest of the caregivers, there were between 2 and 10 data points (mean of 3.2 data points) at which caregiver depression was measured. The time interval from the first to the last observation on caregivers ranged from 4 months to 5 years, with a mean time interval of 1 year. For 20% of all patients, there was 1 data point at which the main independent variable, patient depressive symptoms, was measured; for the rest of the patients, there were between 2 and 10 data points (mean of 4.1 data points) at which patient depressive symptoms were measured. The time interval from the first to the last observation on patients ranged from 4 months to 5 years, with a mean time interval of 2 years. All data points on patients preceded or corresponded to the last data point on their caregivers. We used multilevel analysis to accommodate this flexible observational design.

**Measures**

Descriptive statistics and alphas at baseline, and the mean number of data points for each measure, are displayed in Table 1. Measures on the patients included duration of illness, BADLs and IADLs, and depressive symptoms. No separate measures of cognitive functioning were used because scores on the Mini-Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975) were missing for more severely impaired patients and correlations between MMSE and total scores on ADLs were fairly high (r = -.63).

**Duration of illness** was based on the date of the earliest possible symptoms, as identified by the caregiver in the initial interview with the physician. This date was subtracted from the date of the baseline medical evaluation to compute duration of illness at baseline, which was used as the one measure of duration of illness in all analyses. Mean duration of illness at baseline was 4 years, with a range from 1 year to 11 years.

ADLs were measured with the Cleveland Scale for Activities of Daily Living (Patterson et al., 1992), which is administered by a trained examiner to the caregiver. This scale was designed to measure both BADLs and IADLs in persons with dementia, across the range of dementia severity. The particular strength of this scale is that it includes higher level tasks, such as initiating, planning, and organizing (e.g., “initiates dressing at appropriate times,” “selects clothing,” “prepares bath”), on which persons with early dementia may have deficits. It also includes lower level tasks that are more automatic (e.g., “cleans self,” “feeds self”), on which persons with more severe dementia have deficits. Items are rated on a scale ranging from 0 (completely inde-
Depressive symptoms in the patient were measured by the Consortium to Establish a Registry for Alzheimer’s Disease Behavior Rating Scale for Dementia (BRSD; Mack & Patterson, 1996; Tariot et al., 1995). The BRSD is a structured interview completed by a trained interviewer with the caregiver. The subscale for depressive symptoms includes seven items (feelings of anxiety, sad appearance, hopelessness, crying, guilt feelings, poor self-esteem, and feelings that life is not worth living), plus a follow-up item asking if the person ever made a suicide attempt. It does not include symptoms of altered biological rhythms (e.g., changes in appetite, energy, and sleep) or apathy (e.g., loss of interest and reactivity), which are included in other depression scales (e.g., the Cornell Scale for Depression in Dementia; Harwood, Ownby, Barker, & Duara, 1998). Thus, the BRSD Depressive subscale (BRSDDEP) is mood related and has less overlap with symptoms associated with dementia. Validity of the BRSDDEP has been supported by comparing responses on BRSDDEP items between Alzheimer’s disease patients who were diagnosed as either depressed or nondepressed by use of semistructured clinical interviews (Jacobs, Strauss, Patterson, & Mack, 1998). On the basis of the BRSDDEP score, 70% of the patients were correctly classified as depressed or nondepressed. Caregivers rated BRSDDEP items for frequency of occurrence in the past month from 0 (has not occurred) to 4 (occurred 16 or more days), plus a 0 or 1 for suicide attempt, yielding a possible range from 0 to 29. The mean for BRSDDEP was 4.1, with a range from 0 to 26.

Measures for the caregiver included gender, relationship (spouse vs nonspouse), self-rated health, and the main outcome variable, caregiver depression. Caregivers’ age, race, income, and employment status were not related to caregiver depression at baseline, so they were not included in subsequent analyses. There was a small but significant correlation between caregiver education and caregiver depression at baseline (\( r = -.17, p < .01 \)), but caregiver education was not included in the analyses in order to reduce the number of independent variables. Coresidence of the caregiver and patient was highly correlated with being a spouse \( (r = .60) \), so spouse–nonspouse was used in the analysis.

Self-rated health was rated by a single item asking caregivers to rate their own health, from 1 (excellent) to 5 (poor). The mean was 2.6, with 45% rating their health as excellent or good and 20% rating it as fair or poor.

Depression in the caregiver was measured by the Center for Epidemiologic Studies—Depression scale (CES–D; Radloff, 1977), one of the most frequently used measures of depression among caregivers (Schulz et al., 1990). Caregivers were asked to rate the frequency with which they experienced each of 20 depressive symptoms during the past week from 0 (less than one day) to 3 (5–7 days), with a possible range from 0 to 60. Scores of 16 or above suggest that an individual is at risk for clinical depression. The mean was 12.6, with a range from 0 to 52. Thirty-one percent of the sample scored at baseline in the range at risk for clinical depression.

Mean caregiver depression at each annual visit is given in Table 2. First, means for each pair of consecutive annual visits (0–1, 1–2, 2–3, 3–4, and 4–5) are shown for caregivers with valid CES–D scores on each pair of years. These means show the change in depression over a 1-year interval for the caregivers who were observed over that interval. Second, means at each annual visit are given for all caregivers who were observed in a given year. Neither set of means shows any clear-cut pattern of aggregate change in depression. There is considerable variation between caregivers in rates of change in depression that is hidden by these aggregate means, as is seen.

**Statistical Analysis**

The research objective was to investigate the effects of patient depressive symptoms on the repeated measures of caregiver depression, controlling for duration of illness, dependency in IADLs and BADLs, relationship (spouse–nonspouse), caregiver gender, and caregiver self-reported health. Hierarchical modeling or multilevel analysis (Bryk & Raudenbush, 1992; Goldstein, 1995) was selected to analyze the changes in depression. Multilevel analysis was chosen instead of repeated measures analysis of variance because the former specifies more directly the parameters of growth and change and the determinants of these parameters (Bryk & Raudenbush, 1992, p. 133). Multilevel analysis also allows the use of repeated measures where both the number of observation points and the intervals between the points vary across the units of analysis (i.e., caregivers). This feature makes it possible to use all available data instead of restricting the analysis to cases that have the same number of observations. It is even possible to include cases with only one observation, as we have done, although these cases contribute very little to the longitudinal part of the analysis (Snijders & Bosker, 1999, p. 181). Equations 1–4 illustrate a multilevel model for repeated measures.

### Table 2. Mean CES–D Scores (and n) at Each of Two Consecutive Annual Visits

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**Notes:** Quarterly measures are excluded from this table, and thus the n’s do not reflect the total number of observations used in the multilevel models. CES–D = Center for Epidemiologic Studies–Depression scale.
$Y_{ij} = \beta_{0i} + \beta_{1i}t_{ij} + \beta_{2i}t_{ij}^2 + e_{ij}$  \hspace{1cm} (1)

$\beta_{0i} = \gamma_{00} + \gamma_{01}X_{1i} + \ldots + \gamma_{07}X_{7i} + u_{0i}$  \hspace{1cm} (2)

$\beta_{1i} = \gamma_{10} + \gamma_{11}X_{1i} + \ldots + \gamma_{17}X_{7i} + u_{1i}$  \hspace{1cm} (3)

$\beta_{2i} = \gamma_{20} + \gamma_{21}X_{1i} + \ldots + \gamma_{27}X_{7i} + u_{2i}$  \hspace{1cm} (4)

Equation 1 is a within-person equation for $Y_{ij}$, caregiver depression for person $i$ measured at occasion $j$. In Equation 1, $Y_{ij}$ is a nonlinear function, named a quadratic function, of time $t_{ij}$. The term $t_{ij}$ indicates the time in years from the first occasion of measurement to each subsequent occasion, where $j = 1$ to $m_i$ and $m_i$ equals the number of occasions, which varies from caregiver to caregiver. Thus, $t_{i1} = 0$ for the first occasion and, for example, $t_{i2} = 1.1$ if the second measure occurred 1.1 years later. The term $e_{ij}$ is the residual of $Y$ for each caregiver at each point in time. The coefficients $\beta_{0i}$, $\beta_{1i}$, and $\beta_{2i}$ are the $Y$ intercept, the linear slope or rate of change, and the acceleration of the rate of change, respectively, for each caregiver $i$. Thus, there are 353 different estimates for each coefficient. In other words, Equation 1 is actually 353 different equations, one for each caregiver.

Because the $Y$ intercept is the prediction of $Y$ when $t = 0$ (first measurement), $\beta_{0i}$ equals a caregiver’s predicted depression at the beginning of his or her participation in the project. The variance of $\beta_{0i}$ across the 353 caregivers is the between-person variance of $Y_{ij}$. The variance of the $m_i$ measures of $Y_{ij}$ for each caregiver around each caregiver’s mean $Y_i$ equals the within-person variance.

$\beta_{1i}$ is the rate of change in caregiver depression at $t = 0$. To interpret the rate of change at a specific point in time such as $t = 0$, imagine that $t$ increases by an infinitesimal amount from that point. The product of $\beta_{1i}$ and this infinitesimal change in $t$ equals the amount that $Y$ will change. Thus, $\beta_{1i}$ is the instantaneous rate of change at $t = 0$. If $\beta_{1i}$ is positive, the caregiver’s depression is instantaneously increasing at baseline; if $\beta_{1i}$ is negative, the caregiver’s depression is decreasing.

In a nonlinear function such as the quadratic function (Equation 1), the rate of change itself changes as $t$ changes. $\beta_{2i}$ indicates the acceleration or deceleration of the rate of change in caregiver depression. It determines the change in the rate of change. In Figure 1A, $\beta_{1i} = 2$ and $\beta_{2i} = -1$. Thus, the initial rate of change is positive or increasing. The negative acceleration parameter, however, means that the rate of increase decreases or decelerates as $t$ increases. For example, the curve is steeper between A and B than between B and C. At C, however, the rate of increase equals 0, and beyond C it becomes negative. The negative acceleration parameter results in an acceleration of the rate of decrease as $t$ increases beyond $t = 1$. In Figure 1B, there is an initial negative rate of change. The positive acceleration parameter decreases or decelerates the rate of decrease up to $t = 1$. Beyond $t = 1$, $Y$ has a positive rate of increase, which accelerates as $t$ increases further.

As indicated above, $\beta_{0i}$ and $\beta_{1i}$ represent the level of depression and the rate of change in depression at baseline, $t = 0$. If we wanted to evaluate $\beta_{0i}$ and $\beta_{1i}$ at a time later than $t = 0$, we could subtract some reference value $t_0$ from $t$ and include $t_{ij} - t_0$ in Equation 1. With $t$ “centered” on $t_0$, $\beta_{0i}$ and $\beta_{1i}$ would indicate the level of depression and the rate of change in depression at $t_{ij} = t_0$. One value that is often used to center variables is the grand mean, in this case, $\bar{t}$. Not all caregivers, however, have been observed long enough for them to have a value of $t_{ij} = \bar{t}$; some, for example, are measured only at $t = 0$. Therefore, we have chosen not to center $t$ at the grand mean. Another value that is sometimes used to center variables in multilevel analysis is the within-unit mean, in this case $\bar{t}_u$, the mean time for caregiver $i$. The consequence of centering on $\bar{t}_u$ is that we would be evaluating $\beta_{0i}$ and $\beta_{1i}$ at different times for different caregivers, and the fit of the model when $t$ is centered on $\bar{t}_u$ is different than the fit when it is centered on $\bar{t}$. The way we have chosen to center the data is described in Snijders & Bosker (p. 81). Snijders and Bosker stated that within-unit mean centering should be avoided unless there is a clear theory that the relative score ($t_{ij} - \bar{t}_u$) and not the absolute score ($t_{ij}$) is related to $Y$. Because we do not believe that relative time is theoretically justified, we used the uncentered $t_{ij}$.

The three parameters of our quadratic model of change, $\beta_{0i}$, $\beta_{1i}$, and $\beta_{2i}$, are the focal parameters used to describe each caregiver’s depression. Because there are no time-varying covariates included in Equation 1, these are unadjusted estimates for each caregiver and serve as the dependent variables in Equations 2–4. The objective of this study was to determine whether the patient’s depressive symptoms help explain the between-person variance of $\beta_{0i}$, $\beta_{1i}$, and $\beta_{2i}$, that is, variance in initial caregiver depression (the intercept) and variance in the rate of change and acceleration of change in caregiver depression. Equations 2–4 show these parameters expressed as a linear function of seven independent variables, $X_{1i}$, . . . , $X_{7i}$. These variables are a dummy variable for caregiver gender (female = 1), a dummy variable indicating whether the caregiver is a spouse of the patient (spouse = 1), a self-report of the caregiver’s health at baseline, the duration of AD at the time of the patient’s first assessment, one of the parameters that describes change in the patient’s IADLs, one of the parameters for change in the patient’s BADLs, and one of the parameters for change in patient depressive symptoms (BRSD-
The terms $u_{0i}$, $u_{1i}$, and $u_{2i}$ are the residuals of $\beta_{0i}$, $\beta_{1i}$, and $\beta_{2i}$, respectively, for each caregiver.

The independent variables ($X_{1i}$, \ldots $X_{7i}$) are not identical in each equation. Caregiver gender, spouse–nonspouse, caregiver health, and duration of illness were included in each of Equations 2–4. The measures of IADL, BADL, and BRSDDEP were different in each equation, based on the following steps. First, we estimated the three parameters of Equation 1 for each of these three patient measures. Thus, each patient had an estimate of the initial level, the rate of change, and the acceleration of change of IADL, BADL, and BRSDDEP. That is, we estimated the three parameters of the quadratic model of change for each patient on each of the three variables. An appropriate parameter was selected for each variable to be used in predicting the caregiver depression parameters, as follows. We used the initial levels ($\beta_{0i}$) of IADL, BADL, and BRSDDEP to predict the initial level of caregiver depression (Equation 2); we used the rate of change ($\beta_{1i}$) in IADL, BADL, and BRSDDEP to predict the rate of change in caregiver depression (Equation 3); and we used the acceleration ($\beta_{2i}$) of IADL, BADL, and BRSDDEP to predict the acceleration of caregiver depression (Equation 4).

Although we did not center the time variable for the reasons given above, $X_{1i} - X_{7i}$ were each centered at their mean in order to improve the interpretation of the coefficients $\gamma_{00}$, $\gamma_{10}$, and $\gamma_{20}$. Because these gammas indicate the baseline value, rate of change, and acceleration of caregiver depression when all of the $X$s equal 0, if the $X$s are centered, the gammas equal these parameters of change when all $X$s are at their means. The means of the dummy variables gender and spouse–nonspouse indicate the proportion of cases that are coded 1, thus, $\gamma_{00}$, $\gamma_{10}$, and $\gamma_{20}$ represent proportionately weighted averages of these parameters for men and women and for spouses and nonspouses, adjusted for the other $X$s.

Multilevel models for repeated measures assume that missing values of $Y_{ij}$ are “missing at random.” This means that missing values may be related to previous measures of caregiver depression ($Y_{ij}$) and to the covariates included in the model ($X_{1i}$, \ldots $X_{7i}$), but otherwise must be randomly missing (Hedeker & Gibbons, 1997). In this study, missing values are primarily due to differences between caregivers and patients in the duration of their participation in the study. Variance in the number of observations and the total time of participation is certainly related to the covariates (e.g., duration of illness) and to measures of the caregiver’s depression. It is a rather strong assumption, however, that missingness is otherwise random.

Variables representing patterns of missing values may be included in the models to control for nonrandom missingness (Hedeker & Gibbons, 1997; Little, 1995). Because of our desire to avoid overburdening an already complex model, we elected to represent variance in missing values with a single variable, the mean time of observation of each caregiver ($\bar{t}_{i}$). Mean $t$ is highly correlated with the total time of observation ($r = .983$) and the number of observations ($r = .832$). We centered $\bar{t}_{i}$ at 1.63 years, a value halfway between the minimum and maximum values of $\bar{t}_{i}$. The method of including mean $t$ in the model is shown in Equations 2a–4a.

Equations 2a–4a include a term for the main effect of $t_{i}$ (e.g., $\gamma_{1i}$) and one for its interactive effect with one $X$ (e.g., $\gamma_{1i}X_{7i}$). The main effect indicates the effect of $t_{i}$ when $X$ is at its mean, and the interactive effect represents the change in the effect of $X$ as $t_{i}$ varies. If the effect of either $t_{i}$ or $t_{i}X_{7i}$ is significant, it means that the variance in missing values ($\bar{t}_{i}$) is not random. The main effect of $X$ (e.g., $\gamma_{0i}X_{7i}$) now equals its effect when $\bar{t}_{i}$ is at its centered value (1.63). The first step in testing $t_{i}$ is to enter it into each of Equations 2a–4a in order to examine any main effects it may have. Because we are focusing on the effects of patient depression, a term representing the interaction of BRSDDEP with $\bar{t}_{i}$ is then included in each equation. For example, we include the product of $\bar{t}_{i}$ and the baseline value of BRSDDEP in Equation 2a, the product of $\bar{t}_{i}$ and the rate of change in BRSDDEP in Equation 3a, and the product of $\bar{t}_{i}$ and the acceleration of BRSDDEP in Equation 4a. We also do the same for IADL and BADL, the patient control variables that may change over time. We do this one at a time for IADL, BADL, and BRSDDEP because otherwise there would be 12 terms involving $\bar{t}_{i}$ in the model.

We used the MLwiN software (Prosser, Rasbash, & Goldstein, 1991) for multilevel analysis to estimate the parameters of our repeated measures models. MLwiN uses an iterative generalized least squares algorithm that provides consistent estimates of model parameters and standard errors. An alternative algorithm is also available to obtain restricted or unbiased estimates of the model parameters in small samples. As both algorithms provided similar estimates for our models, we report the more commonly used unrestricted estimates for presentation purposes. Bryk and Raudenbush (1992, p. 50) recommended comparing the parameter estimate divided by its standard error ($\hat{\gamma}/\hat{\sigma}$) to the $t$ distribution rather than the normal distribution for inferential purposes.

**Results**

The bivariate correlations at baseline of the variables included in the multilevel analysis are displayed in Table 3. Looking first at the patient variables, as would be expected, longer duration of illness is related to greater dependency in both BADLs and IADLs. Although there is relatively high collinearity between dependency in instrumental and basic activities at baseline ($r = .71$), which increases their standard errors as predictors of caregiver depression, the correlations between the rate of change of instrumental and basic dependency and the acceleration of change of instrumental and basic dependency are only .20 and .21, respectively (not shown). Patient depressive symptoms are negatively related
to BADLs (−.11), which indicates patients with greater BADL impairment are somewhat less depressed. A possible reason for this negative correlation is that basic BADL impairment tends to occur at a later stage in the progression of dementia, when patient depressive symptoms are less, as some studies have shown (Katz, 1998; Payne et al., 1998). This negative correlation, however, could be due to other confounding factors, such as decline in ability to express depressive thoughts as the disease progresses. Among the patient variables, the only ones related to caregiver depression were duration of illness (β1), and depressive symptoms (β2). Among the caregivers, however, larger than the within-patient variance for each variable in both Models 2 and 3. Thus, there is significant between-patient variance in the rate of change and acceleration of both basic and instrumental dependency and of depressive symptoms.

The covariances between the parameters of change for each of the three patient variables are indicated by γi, respectively. Each of these variances is significant for each variable in both Models 2 and 3. Thus, there is significant between-patient variance in the rate of change and acceleration of both basic and instrumental dependency and of depressive symptoms.

The mean time of observation (t̄) has a negative effect on the rate of increase of dependency in both types of ADLs (−0.89 and −1.33 for IADL and BADL, respectively, in Model 3), indicating that the initial rate of increase of ADL dependency is lower for those who were observed longer. These negative effects of t̄ suggest that lower rates of increase in ADL dependency may delay nursing home placement and thus increase the time of participation in the study. Mean time of observation, however, positively affects the acceleration of IADL dependency (0.11) but not BADL dependency. Thus, the longer the patient was studied, the less the deceleration of the rate of increase in IADL dependency.

The positive effect of t̄ on IADL acceleration, but not BADL acceleration, may indicate that caregivers expect or are able to tolerate accelerating IADL dependency (e.g., needing help in travel, shopping, using the telephone). Without accelerating dependency in bathing, dressing, and toileting, the patient remains in the community and caregivers thus continue in the study.

More important than whether the mean rate and the mean acceleration of patient variables are significantly different than zero is whether these parameters vary significantly between patients. The between-patient variance in Time 0 measurement, rate of change, and acceleration are indicated in Table 4 by σ20i, σ21i, and σ22i, respectively. Each of these variances is significant for each variable in both Models 2 and 3. Thus, there is significant between-patient variance in the rate of change and acceleration of both basic and instrumental dependency and of depressive symptoms.

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The covariances between the parameters of change for each of the three patient variables are indicated by γi.
The covariance across patients between the rate of change and the acceleration of change ($\sigma_{u_1u_2}$) is significantly less than zero for all three variables ($\sigma_{u_0} = 0.33$, $\sigma_{u_1} = 0.44$, and $\sigma_{u_2} = 0.22$). This indicates that the greater the rate of increase in IADL, BADL, and BRSDDEP, the less the acceleration in these variables. Thus, when the increase in each variable is rapid initially, it tends to slow or even level off over time.

The values of $u_0$, $u_1$, and $u_2$ (patient residuals as shown in Equations 2–4) were generated by Models 2–3 in Table 4 for the measurement at Time 0, the rate of change, and the acceleration of change, respectively. These residuals indicate how much each patient deviates from the mean value of each parameter of change (adjusted by $t_i$ in Model 3). A positive $u_1$ for IADL dependency, for example, would indicate that a patient had a higher than average rate of increase in this kind of dependency. A negative $u_1$ would indicate a slower than average rate of increase. The mean of each residual variable equals 0 ($\sigma_{u_0} = 0.05$, $\sigma_{u_1} = 0.44$, and $\sigma_{u_2} = 0.22$). The residuals for IADL and BADL from Model 3 and for BRSDDEP from Model 2 were used as independent variables in the model for changes in caregiver depression.

Table 5 contains the estimated parameters of four models for caregiver depression, namely, the within-caregiver means model (Model 1), the model for the means of the parameters of change (Model 2), a model with the independent variables as predictors of the parameters of change as specified by Equations 2–4 (Model 3), and a model with the independent variables plus the mean time of observation as specified by Equations 2a–4a (Model 4). Model 1 shows that there is greater variance in depression between caregivers (65.299) than over time within caregivers (28.062), as was the case with the three patient variables. However, both sources of variance are significant. Model 2 shows that the average caregiver, unlike the average patient, has a rate

![Figure 2. Changes in patient depression and dependency at $t_i = 1$. BADL = basic activities of daily living; IADL = instrumental activities of daily living; BRSDDEP = Behavior Rating Scale for Dementia Depressive Subscale.](attachment:image.png)
of increase in depression that is significantly different than zero (1.359). The average value of the acceleration parameter (−.166), however, is not significant. Thus, on average, caregivers are characterized by a positive rate of increase in depression across the observed occasions, with little or no deceleration of that increase. Both the rate of change ($\beta_1$) and the acceleration of change ($\beta_2$), however, vary significantly across caregivers (14.622 and 0.811, respectively). Furthermore, there is a significant negative covariance ($\sigma_{u0u2}$) between the rate of change and the acceleration of change (as was the case with the three patient variables). That is, caregivers with high rates of increase in depression (positive $\beta_1$'s) tend to have low acceleration or deceleration (negative $\beta_2$'s) in depression. The addition of $i \cdot t$ to Model 2 was not significant (not shown).

Turning to Model 3 in Table 5, we see that six out of seven independent variables have significant effects on caregiver depression at Time 0. Females, spouses, and care-
givers with poor health are significantly more depressed at the baseline measurement. The shorter the duration from onset of AD to entry into the study, the more depressed is the caregiver initially. The initial levels of IADL dependency and of patient depressive symptoms are also significantly related to caregiver depression; the greater the patient’s IADL dependency and depression, the greater the caregiver’s baseline depression. The baseline measure of BADL, however, is not significantly related to depression independently of baseline IADL.

None of the caregiver variables are significantly related to the rate of change in caregiver depression. The rate of change in the patient’s IADL dependency at Time 0 (0.271) and the rate of change in the patient’s depressive symptoms at Time 0 (0.402), however, have significant positive effects on caregiver depression (for patient depressive symptoms, \( t = 1.869, p = .031 \), one-tailed, not shown). The greater the rate of increase in the patient’s IADL dependency and depressive symptoms, the greater the rate of increase in the caregiver’s depression.

With respect to the acceleration of caregiver depression, acceleration in both IADL (0.505) and BADL (0.219) dependency has significant positive effects on caregiver depression. The greater the acceleration in IADL and BADL dependency, the more the change in caregiver depression accelerates. This is despite the earlier finding that the initial level and the rate of change in BADL at baseline were not significantly related to caregiver depression. Acceleration of patient depressive symptoms, however, is not significantly related to acceleration of caregiver depression.

We now discuss the results of including \( \tilde{t}_i \), centered at 1.63, in the model in order to control for nonrandom missing values. As previously outlined, \( \tilde{t}_i \) was first entered in Equations 2–4 to test its main effects. The addition of \( \tilde{t}_i \) did not significantly improve the fit of the model, \( \chi^2 (3, N = 353) = 1.065, p = .786 \) (estimated parameters not shown). Model 4 in Table 4 gives the estimated parameters specified by Equations 2a–4a for the three interactions involving \( \tilde{t}_i \times BRSDDEP \). The addition of the three interaction terms resulted in a slight but significantly improved fit, \( \chi^2 (3, N = 353) = 7.665, p = .054 \). Of the three possible interactions, only the positive \( \gamma (.693) \) for \( \tilde{t}_i \times \beta_1 \) (BRSDDEP) reached significance. This means that the longer the time the caregiver was observed, the greater the positive effect of the initial rate of change in patient depressive symptoms on caregiver depression. The direction of this interaction is counter to what we would have expected, which is that caregivers who become the most depressed by a rapid increase in their family members’ depressive symptoms would not stay in the study as long as caregivers who are less affected by their family members’ depressive symptoms. In other words, we would have expected a negative interaction, if any. The main effect of the rate of increase in patient depressive symptoms, which is evaluated at \( t = 1.63 \), is positive and significant (.589).

The addition of three interaction terms for \( \tilde{t}_i \times IADL \) did not significantly improve the model’s fit, \( \chi^2 (3, N = 353) = 2.312, p = .510 \); it was necessary to use the restricted generalized least-squares algorithm to obtain an iterated solution for this model. Neither did the addition of three terms for the \( \tilde{t}_i \times BADL \) interaction, \( \chi^2 (3, N = 353) = 0.670, p = .880 \). Thus, there is no evidence that the effect on caregiver depression of patient ADL dependency is related to how long the caregiver participated in the study.

We conducted 12 tests for the effect of \( \tilde{t}_i \), to wit, three main effects and nine interactions. Only one was significant \( \tilde{t}_i \times \chi_1 \) (BRSDDEP), and this interaction is counter what we would have reasonably expected. Therefore, we believe that this result should be treated cautiously. With the single exception of this interaction, the results for Model 4 are nearly identical to those for Model 3.

We examined interaction effects for IADL \( \times \) BRSDDEP and BADL \( \times \) BRSDDEP to see if the effects of patient depressive symptoms depended on the degree of patient dependency in IADLs and BADLs, and vice versa. These interactions were tested for the baseline measures, the rates of change, and the accelerations of these variables for a total of six tests. The only significant result was a negative interaction between the accelerations of patient depressive symptoms and patient dependency in basic activities, \( \beta_2 (BRSDDEP) \times \beta_2 (BADL) \) (not shown). This indicates that the greater the acceleration of patient depressive symptoms, the less the effect of acceleration of BADL dependency on caregiver depression, and vice versa (i.e., higher acceleration of BADL dependency reduces the effect of acceleration of BRSDDEP). We should be cautious about this interaction, however, because it is the only one of these six tests that reached significance and because nine additional interactions (those involving \( \tilde{t}_i \), just discussed) have also been tested, of which only one was significant.

We have found that changes in patient IADL and BADL dependency and in patient depressive symptoms affect changes in caregiver depression. To examine more precisely the pattern of these effects over time, Figure 3 shows trends in caregiver depression as a function of average, high, and low initial rates of change in patient depressive symptoms. In Figure 3A, the values of the parameters for the constant terms of Model 4 in Table 5 are used for \( \beta_0, \beta_1, \) and \( \beta_2 \). Because each of the \( \chi_i \)s is centered at its mean and \( \tilde{t}_i \) is centered at 1.63, these parameters represent the baseline depression, the initial rate of change in depression, and the acceleration of depression for an average caregiver who has a mean observation time of 1.63 years. With these values of the betas, we plotted the quadratic model of change (Equation 1) over a period of 6 years. The maximum number of years that caregiver depression was measured is 5.2 years; only 5% of the 353 caregivers were followed for 4 years or longer. Thus, the trend shown beyond the 4th or 5th year in the plots may not be valid. Nevertheless, the first plot shows that caregivers who are average on all of the independent variables are expected to have monotonically increasing levels of depression throughout most of the period. The rate of increase, however, slows as time passes. The most rapid increase of caregiver depression is in the first years, and the increase slows sufficiently to show no further increase by 5.6 years.

Figure 3B illustrates the effect of a high rate of increase in patient depressive symptoms (a high rate is defined as one standard deviation above the mean of \( \beta_2 \) on change in caregiver depression. Mean values of all other variables, except \( \tilde{t}_i = 1.63 \), were used to generate the expected parameters of
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change in caregiver depression. The plot shows monotonically increasing caregiver depression throughout the entire period. Unlike the trend in Figure 1A, average deceleration is insufficient to cause a leveling off of caregiver depression during the 6 years. In fact, the curve would not peak until 9.2 years.

The third graph (Figure 3C) is based on a low rate of growth in patient depressive symptoms (one standard deviation below the mean). Although it shows a slight overall decrease in caregiver depression, there is little or no change in caregiver depression during the first 4 years.

Figure 4 shows analogous plots evaluated at high and low rates of change in IADL dependency. The curves in Figures 4A and 4B are virtually identical to those in Figures 3B and 3C. Thus, variance in the initial rate of change in IADLs and in patient depression have the same effect on changes in caregiver depression.

**DISCUSSION**

To summarize, the focus of this study was the effects, over time, of depressive symptoms in persons with AD on depression in their family caregivers. Additional variables accounted for were duration of illness, patient dependency in BADLs and IADLs, relationship (spouse or nonspouse), caregiver gender, and self-reported health. The effects of these variables on baseline caregiver depression, the linear rate of change in caregiver depression, and the acceleration of the rate of change in caregiver depression were evaluated using multilevel analysis (see Model 3 in Table 5). As hypothesized, more patient depressive symptoms predicted greater caregiver depression at baseline, and an increasing rate of change in patient depressive symptoms predicted an increasing rate of change in caregiver depression; however, counter to the hypothesis, acceleration in patient depressive symptoms did not predict acceleration in caregiver depression.

Additional predictors of caregiver depression at baseline were shorter duration of illness and greater patient dependency in IADLs, but not BADLs. The effects of these two patient variables were not expected, but they point to the need to intervene early with caregivers who may be depressed by the initial realization of their family members’ illness and early signs of decline. Caregiver variables that predicted caregiver depression at baseline were being a female caregiver, being a spouse rather than a nonspouse, and being in poor health themselves, as expected. In predicting the rate of change in caregiver depression, only one variable in addition to patient depressive symptoms was a significant predictor; increasing rate of change in patient dependency in IADLs predicted increasing rate of change in caregiver depression. Acceleration of the increase in caregiver depression was predicted by acceleration in patient dependency in IADLs and BADLs.

Different rates of change in initial patient depressive symptoms were examined for their effects on patterns of change in caregiver depression (as shown in Figure 3). If caregivers experienced the average rate of change in all independent variables, their initial depression increased rapidly in the first 2 years, continued to increase slowly, and then leveled off at about 5 years. However, if patient depression was increasing at a high rate (and all other variables were held at their means), caregiver depression initially increased rapidly, continued to increase, and leveled off later. On the other hand, if patient depression increased at a low rate, there was little or no change in caregiver depression during the first 4 years. Tracking rates of change in patient IADL dependency (as shown in Figure 3), a change that occurs early in the illness, showed a similar pattern of effects on caregiver depression.

To conclude, results of this study add a seldom-examined patient characteristic, depressive symptoms, to the list of what have been called primary stressors (Aneshensel et al., 1995) that contribute to caregiver depression. More patient
depressive symptoms were associated with caregiver depression at baseline, and an increase in patient depressive symptoms was associated with an increase in caregiver depression. These findings support the findings of the few other investigators (Brodaty & Luscombe, 1998; Drinka et al., 1987; Hadjistavropoulos et al., 1994) who have reported an association between patient depressive symptoms and caregiver psychological morbidity or burden. They are also consistent with the results of Tower and Kasl (1996), who found, among a probability sample of community-dwelling older adults, that depressive symptoms in one older spouse influence depressive symptoms in the other, both cross-sectionally and longitudinally. Their findings were stronger when couples were close and held when known intrapersonal risk factors and the health status of the spouse were controlled for.

Tower and Kasl (1996), in their discussion of why depression in one spouse might contribute to depression in the other, gave insights into what might be happening between caregivers and the person with dementia for whom they care, especially if they have a close relationship. Extrapolating from Tower and Kasl, it seems that persons with dementia who exhibit depressive symptoms are likely to be negative about the present and future, make critical comments, and express little appreciation of their caregivers. Like spouses of depressed persons in general, female caregivers of depressed family members may feel increased loneliness and a sense of futility about their efforts to help; male caregivers may feel inadequate and helpless. All these negative interactions and thoughts can contribute to a downward spiral of depression for the caregiver.

The findings from the present study support the importance not only of patient depressive symptoms in understanding caregiver depression, but of patient characteristics in general, including the early phase of the illness and the rate of increase in initial dependencies. As patients became more dependent in IADLs, usually the skills most sensitive to early cognitive deficits, they needed more reminders, supervision, and guidance with complex tasks such as traveling and shopping. The more rapidly these changes occurred, the more depressed were the caregivers, even controlling for patient depressive symptoms. The more rapidly these changes occurred, the more depressed were the caregivers, even controlling for patient characteristics. Except for Aneshensel and colleagues (1995), no investigators of caregiver well-being have addressed the rate of change in patient characteristics, and this has led to the underestimation of the importance of patient characteristics in the stress process. As Aneshensel and associates concluded, the patient’s impairment is central in the stress process experienced by caregivers, especially the rate at which the patient declines over time.

Limitations of the present study include the focus on one type of patient behavior problem, depressive symptoms. Although depressive symptoms are the most frequently occurring problem, other less frequent behaviors, such as disruptive behaviors, should be examined for their relative contribution to caregiver depression.

Significant strengths of this study include a sample of patients who were carefully diagnosed and well characterized. The Cleveland Scale for Activities of Daily Living (Patterson et al., 1992) proved to be highly sensitive to functional changes early in dementia, and this likely accounts for the strong effect of patient dependency in IADLs on caregiver depression. The Consortium to Establish a Registry for Alzheimer Disease BRSD (Tariot et al., 1995), with its Depressive Symptoms subscale, picked up mood changes in patients separate from the vegetative symptoms and apathy that confound depressive symptoms with symptoms of dementia. Its sensitivity to mood changes early in dementia, again, probably contribute to the effect of rate of change in depressive symptoms on depression. Finally, rather than summing across the wide range of behavioral symptoms exhibited in persons with dementia, and ignoring their ebb and flow over the course of the illness, we chose to focus on one pattern of symptoms, patient depressive symptoms, and the changes in them.

Findings from this study suggest that treatment of patient depressive symptoms may improve the quality of life for patients and for their family caregivers. They also support interventions for caregivers early in their family members’ illness when caregivers’ depression may be high due to their family member’s depressive symptoms and initial signs that their family member is becoming more dependent.

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