

Onset, timing and risk for depression and anxiety in family caregivers to heart transplant recipients

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ABSTRACT

Background. Family members adopt key caregiving roles in the maintenance of transplant recipients' health. While the bulk of the caregiving literature suggests that rates of psychiatric disorder should be high in these caregivers, the potential benefits of transplantation may instead lead to less distress than in other caregiving situations. We examined prevalence and risk factors for depressive and anxiety-related disorders in caregivers throughout 3 years after their family member's heart transplant.

Method. A total of 190 caregivers (97% of eligible respondents) were enrolled. They received psychiatric and psychosocial evaluations at 2, 7, 12 and 36 months post-transplant. Survival analysis determined cumulative rates of psychiatric disorders and the impact of potential risk factors.

Results. Rates of depressive and anxiety-related disorders met or exceeded other caregiver populations' rates. By 3 years post-transplant, cumulative onset rates were: Major Depressive Disorder (MDD), 31.6%, Adjustment disorders, 35.4% (29.4% with anxious mood); Post-Traumatic Stress Disorder related to the transplant (PTSD-T), 22.5%, Generalized Anxiety Disorder, 7.3%, and any assessed disorder, 56.3%. PTSD-T occurred primarily during the first year post-transplant. Other disorders' rates increased over the entire study period. Risk for disorder was elevated by positive lifetime history of psychiatric disorder, greater post-transplant caregiving responsibilities, and a poorer relationship with the patient. Risk for MDD was further increased by caregiver unemployment, and risk for anxiety disorders was further increased by younger age, low sense of personal mastery, and high use of avoidance coping strategies.

Conclusions. Transplantation is associated with costs and benefits for not only patients but family caregivers. Caregivers' risk for psychiatric illness should be considered when developing interventions to promote families' long-term adjustment to the transplant process.

INTRODUCTION

Transplantation of the kidneys, liver, heart, lungs, pancreas, and bone marrow can significantly extend the lives of patients with a variety of end-stage diseases. These procedures are

becoming increasingly commonplace, particularly in North American and Western European countries, where they serve as the therapies of choice for enhancing end-stage disease patients' functional capacity and quality of life (QoL). Significant costs as well as benefits may accrue in the aftermath of transplantation. Both the costs and cost effectiveness in terms of health-care resource allocation, societal burden broadly

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defined, and specific patient outcomes continue to receive intensive attention (Dew *et al.* 1997*b*; Bravata *et al.* 1999; Wainwright *et al.* 1999; van Agthoven *et al.* 2001; Anyanwu *et al.* 2002).

An issue that is generally overlooked in the weighing of costs *versus* benefits of transplantation concerns the fact that, for most transplant recipients, family members adopt key caregiving roles in the maintenance of recipients' health and well-being. In fact, as transplant-related hospital stays decrease and out-patient services continue to constrict due to economic pressures, family caregivers assume increasing responsibility for providing any daily care and assistance that transplant recipients may need (Dew *et al.* 2002). Whether such caregiving has health and/or QoL consequences for the family caregivers themselves constitutes an important, but less visible source of costs (and potential benefits) of transplantation (Dew, 1998*b*; Bunzel *et al.* 1999; Collins *et al.* 2000).

The present study focuses on a key element of caregivers' well-being, namely their mental health, in the years following their family member's receipt of a new heart. Family caregivers' psychological status is of particular concern because it appears to contribute to individuals' social functioning, risk for physical morbidity, and even mortality, in the context of both chronic stressor exposure in general (Kiecolt-Glaser *et al.* 1998; Baum *et al.* 1999; Hirschfeld *et al.* 2000) and caregiving-related stressors in particular (Schulz *et al.* 1995, 1997; Shewchuck *et al.* 1998; Schulz & Beach, 1999; Berg-Weger *et al.* 2000; Da Roza Davis & Cowen, 2001; Vitaliano *et al.* 2002). Moreover, caregivers' mental health influences the care recipients' own health and well-being (Biegel *et al.* 1991; Williamson & Shaffer, 2001; Burgener & Twigg, 2002). However, aside from studies of transplant caregivers' subclinical distress levels, primarily during the early aftermath of transplantation (Chowanec & Binik, 1989; Baumann *et al.* 1992; Erdman *et al.* 1993; Canning *et al.* 1996; Foxall & Gaston-Johansson, 1996; Rodrigue *et al.* 1997; Wicks *et al.* 1998; Boyle *et al.* 2000), there is little evidence regarding the prevalence and important risk factors for clinically significant psychiatric disorder in this population.

Based on a large literature on the mental-health effects of caregiving to individuals with a variety of chronic medical conditions (Gallagher

et al. 1989; Dura *et al.* 1990; Schulz *et al.* 1990, 1995; Eisdorfer, 1991; Cochrane *et al.* 1997; Gillen *et al.* 1998; Nijboer *et al.* 1999; Carter & Chang, 2000; Flaskerud *et al.* 2000; Rabkin *et al.* 2000; Resource Implications Study Group, 2000; Shua-Haim *et al.* 2001), it might be hypothesized that caregivers to transplant recipients would show similarly elevated rates of psychiatric disorders, especially as the period of caregiving extends over a number of years. This hypothesis derives from a conceptual model of the chronic stress process in general – and its specific application in caregiver populations – in which the combined effects of ongoing stressors and strains from multiple domains leads to marked increases in the risk for psychiatric distress and diagnosable disorder (Pearlin & Schooler, 1978; Kessler *et al.* 1985; Pearlin *et al.* 1990; Eisdorfer, 1991; Vitaliano *et al.* 1991; Pearlin, 1994; Turner *et al.* 1995; Haley *et al.* 1996; Baum *et al.* 1999; Dohrenwend, 2000; Schulz *et al.* 2000). In support of this hypothesis are the facts that many of the chronically stressful elements of post-transplant life are similar to those faced by other chronic-illness patients and their families. These stressors include the complex medical regimen, the continued need for medical tests and invasive procedures, and the unpredictability of complications and secondary illness. Yet the aftermath of transplantation also differs fundamentally from the majority of chronic health conditions for which caregiver outcomes have been examined. Rather than the deteriorating course typical in many chronic conditions, in which patient and family changes are often expected to be negative, transplantation more often leads to a marked reversal – or at least a more favorable level of stabilization – of patients' patterns of disability. Indeed, the hallmark of transplantation is its ability to give end-stage disease patients a 'second chance' at life (Simmons *et al.* 1987; Dew *et al.* 1997*b*). This suggests that the rates of psychiatric distress among family caregivers to transplant recipients may be lower than in other caregiver populations.

Our study provides unique data to address these alternative hypotheses. Advancing beyond the few studies that have examined transplant family caregivers' subclinical psychiatric distress levels, we consider the prevalence of diagnosable psychiatric disorders and the timing of their

Table 1. Background characteristics of 190 caregivers to heart transplant recipients

Caregiver characteristics	Total cohort enrolled (n = 190)	Status at 36-month follow-up			χ^2 3-group comparison
		Panel sample (n = 124)	Refused follow-up or left caregiver role† (n = 33)	Recipient or caregiver death‡ (n = 33)	
Gender, % male	14.7	9.7	15.2	33.3	10.24**
Age, % <50 years	51.1	51.6	48.5	51.5	0.10
Race, % Caucasian	94.7	93.5	96.9	97.0	0.53§
Education, % \leq high school	59.8	54.0	68.8	72.7	5.08
Marital status, % married	93.2	95.2	87.9	90.9	2.86§
Income, % <\$25 000	46.2	44.4	44.8	54.5	1.12
Employment status, % currently employed	56.6	53.7	57.6	66.7	1.81
Occupation, % professional	46.2	44.6	37.5	60.6	3.85
Relationship to recipient, % married	72.1	78.2	54.5	66.7	7.85*

† Includes 22 refusals plus 11 who exited the role of caregiver due to their own or the recipient's decision.

‡ Includes 30 recipients and 3 caregivers who died.

§ Fisher exact *p* levels were calculated due to expected cell sizes of <2 for one or more cells; none were <0.10.

* *p* < 0.05, ** *p* < 0.01.

onset throughout the first 3 years after transplantation. Moreover, in contrast to the bulk of studies of caregivers in general – and caregivers to transplant recipients in particular – that have examined samples of convenience, we consider these issues in a representative caregiver sample. Finally, we examine whether any psychiatric disorder observed in the caregivers could be predicted by the nature and level of burden associated with caregiving, as well as by caregivers' demographic, mental-health history and psychosocial status at the time of their family member's transplant. Potential predictors in these classes were selected (*a*) based on their prominence in conceptual models of both the chronic stress process in general and as it has been applied to caregiver populations, and (*b*) because of empirical evidence of their importance in transplant-related and other caregiving contexts (Schulz *et al.* 1990, 1995, 2000; Biegel *et al.* 1991; Eisdorfer, 1991; Vitaliano *et al.* 1991; Baumann *et al.* 1992; Turner *et al.* 1995; Canning *et al.* 1996; Christensen *et al.* 1998; Yates *et al.* 1999; Beach *et al.* 2000; Dew *et al.* 2000; Grant *et al.* 2000; Cannuscio *et al.* 2002; Edwards *et al.* 2002; Powers *et al.* 2002).

METHOD

Respondents

A total of 190 caregivers to heart transplant recipients were enrolled in a prospective study spanning the first 3 years after the transplant.

The heart recipients included all adults (aged 18 years or older) who received transplants between July 1989 and July 1995 in the Cardiothoracic Transplantation Program, University of Pittsburgh Medical Center. Eligible caregivers were identified by asking these recipients to name the family member who gave them the greatest amount of daily care and assistance. The sample of 190 caregivers constituted 97% of eligible caregivers (six refused to participate). Respondents were indistinguishable from the few non-respondents on demographic characteristics and their family member's cardiac-related health history. During the 3 years after their family member's transplant, 22 caregivers (11.6%) refused to continue in the study. In addition, because our focus was on those who maintained the caregiving role during the study period, we did not re-interview 11 (5.8%) who ended their caregiving role due to their own or the recipient's decision, or 30 caregivers (15.8%) whose recipient died during the study period. Finally, three caregivers (1.6%) died during the follow-up period. Our analyses of prevalence rates of psychiatric disorders include data from all individuals until they were lost to follow-up.

Demographic and background characteristics of caregivers with complete follow-up data, those who left the study due to their own or the recipient's decision, and those who exited the caregiver role due to their own or the patient's death are shown in Table 1. The majority of caregivers were married women. They ranged

from 18 to 81 years of age (median = 49 years). Caregivers with complete follow-up data were similar to those with incomplete follow-up on most characteristics. The only reliable differences were that respondents who left the caregiver role through their own or the patient's death were more likely to be male, and caregivers with incomplete follow-up due to their own or the recipient's decision were less likely to be heart recipients' spouses. (They tended to be other family members such as adult daughters and mothers.) Considering the entire group of 66 caregivers lost to follow-up for any reason, there was no reliable association between reason for loss to follow-up and time to drop-out, and there was no association between any baseline characteristic in Table 1 (or any other variable examined in the present report) and time to drop-out.

Procedure

The protocol was reviewed and approved by the Institutional Review Board of the University of Pittsburgh. After obtaining written informed consent, individual 90- to 120-min interviews were conducted with caregivers at 2, 7, and 12 months post-transplant. A similar assessment was conducted at the time of the recipient's third anniversary of their transplant. Our rationale for completing multiple, relatively closely spaced interviews during the first year post-transplant derived from the fact that this year is a time of marked change for patients and families alike as they adjust to the patients' new post-transplant medical regimen and physical recovery from the surgery (Dew et al. 2000, 2002). While transplant recipients' health generally reaches a period of stability during the second year after surgery, the third year – and the years thereafter – are characterized by increasing rates of longer-term health problems and complications associated with transplantation (e.g. cancers, chronic graft rejection; Hosenpud et al. 2000; Deng, 2002). Thus, we decided to conduct an additional follow-up interview at 3 years post-transplant in order to chart additional mental health changes in that may have begun to emerge in patients (Dew et al. 2001) and in their caregivers.

At all time-points, interviews were conducted either face-to-face during the heart recipient's routine out-patient follow-up visit, or, if the caregiver did not travel to the Medical Center,

by telephone. The percentage of interviews conducted by telephone increased across the four follow-up time-points (41, 50, 58 and 72%, respectively). This reflected the facts that heart recipients were less likely to return to the Center, and caregivers were less likely to accompany them, as time elapsed post-transplant. There were no systematic differences on the variables included in our analyses between caregivers who were interviewed by telephone and those interviewed face-to-face.

The semi-structured interviews were conducted by clinically trained interviewers with master's or doctoral degrees in a mental-health discipline. They participated in an intensive, comprehensive training program and inter-rater reliability evaluation before conducting interviews, with periodic field checks of inter-rater reliability during the data collection phase of the study. On semi-structured clinical instruments [e.g. the Structured Clinical Interview for DSM-III-R (SCID)], inter-rater reliability levels were maintained at levels exceeding an intra-class correlation of 0.90.

Instruments

Psychiatric status post-transplant

Because depression- and anxiety-related disorders are prevalent in many populations exposed to chronic stressors (Kessler et al. 1985; Dew, 1998b; Baum et al. 1999), including transplantation (Dew et al. 1998b) and family caregiving (Schulz et al. 1990, 1995), we examined specific DSM-III-R disorders (APA, 1987), including Major Depressive Disorder (MDD), Generalized Anxiety Disorder (GAD), Adjustment disorder with depressed and/or anxious mood (post-transplant only), and Post-Traumatic Stress Disorder related to the transplant experience (PTSD-T). With the exception of PTSD-T, discussed below, disorders were assessed with the SCID (Spitzer et al. 1992). The 2-month interview assessed lifetime pre-transplant and early post-transplant history; subsequent interviews covered the period since last assessment. Because the final 36-month interview covered a period substantially longer than any of the other interviews (2 years), we used additional interview strategies that have been shown to maximize the accuracy of individuals' dating of their episodes of distress (Switzer et al. 1999). These included (a) working

backwards chronologically from the present to the past (Loftus *et al.* 1991), and (b) helping respondents to identify autobiographical landmarks in order to link recall to important events in their lives (Friedman, 1993; Lyketsos *et al.* 1994; Hunt & Andrews, 1995).

The SCID is a widely used, state-of-the-art semi-structured interview schedule designed to be administered by trained clinicians (Spitzer *et al.* 1992; Switzer *et al.* 1999). Its psychometric properties for the segments that we administered are well established and are comparable to those of other structured diagnostic instruments (Williams *et al.* 1992). It is designed to include, for each diagnostic category, several stem questions about cardinal symptoms (e.g. for MDD, the stem questions inquire about depressed mood and loss of interest) and duration of these symptoms. If individuals meet thresholds levels of distress on the stem questions, additional questions follow that allow criteria for a diagnosis to be established.

Early in the study, we noted that respondents frequently mentioned symptoms and experiences surrounding the transplant that resembled PTSD. Thus, we broadened our 12-month and 36-month post-transplant interviews to include an assessment of transplant-related PTSD (PTSD-T), adapted from the Michigan version of the WHO/ADAMHA Composite International Diagnostic Instrument (CIDI) (WHO, 1990; Kessler *et al.* 1994), and diagnosed according to the symptom and duration criteria of DSM-III-R. (PTSD was not included in the SCID at the time we assembled our interview.) The CIDI is a fully structured interview (i.e. in contrast to the SCID, interviewers follow a more fixed set of options when probing for additional information for clarification of responses and the response options are more highly constrained). Similar to the SCID, however, the PTSD section is organized so that there are several stem questions. If a respondent endorses the occurrence of a traumatic event, the interviewer inquires about whether the cardinal symptoms of the disorder were present at a threshold level of severity, and the duration and timing of distress is also ascertained. In the present study, the 12-month interview assessed whether PTSD-T-related symptoms occurred during the period 0–7 months post-transplant and/or 8–12 months post-transplant; the

36-month assessment covered the period since prior evaluation.

Potential risk factors for psychiatric disorder post-transplant

In addition to standard demographic and background characteristics (see Table 1), we considered several other categories of variables measured at the 2-month interview, based on previous evidence suggesting that these classes of variables would increase risk for (i.e. influence individuals' likelihood of developing) one or more of the targeted psychiatric disorders post-transplant. These classes included pre-transplant demographic status and psychiatric history; caregiver burden, and social supports and coping styles. While variables such as burden and social supports might be expected to vary somewhat during the course of the 3-year follow-up period, we focused on potential predictors assessed at the initial 2-month evaluation for two reasons. Firstly, from the standpoint of intervention development for transplant families, it is most important to identify early post-transplant risk factors for long-term difficulties, rather than simply identify factors that co-vary with (and therefore could instead be outcomes of) the long-term difficulties over time post-transplant. Secondly, in the case of caregiver burden measures, while burden levels declined over time in the cohort (see Dew *et al.* 1998a for a full description), initial levels of burden were substantially correlated with subsequent levels of burden (median $r=0.45$, interquartile range = 0.42–0.50) and thus served as useful 'proxies' for more detailed modeling of repeated burden assessments and their relationship to mental health.

Pre-transplant demographic status and psychiatric history. These measures included known demographic risk factors for psychiatric disorder (gender, age, education level) (Kessler *et al.* 1994), as well as whether respondents had a lifetime personal history of MDD and/or GAD, assessed as described above. We note that we inquired at the 2-month post-transplant interview separately about personal history of these disorders during both the waiting period for transplant (the period when the patient would have been most disabled by their illness

and in need of assistance) and during the years prior to the initial evaluation for transplant. (The evaluation for transplant marked the formal beginning of the waiting period.) However, we created only a single variable to reflect the presence of disorder at any point prior to the patient's transplant (i.e. during the waiting period for earlier) for several reasons: (a) all but a handful of individuals had experienced onsets of disorder well prior to the patient's evaluation for transplant, making it unreasonable from an analytical standpoint to construct separate variables reflecting earlier lifetime history *versus* history during the waiting period, and (b) the length of the waiting period for transplant varied dramatically from a few days to several years. For this latter reason alone, creation of a variable reflecting psychiatric disorder during the waiting period would not have been highly meaningful since the denominator of 'time' would have varied too widely between individuals to interpret what the presence or absence of disorder in a given caregiver actually signified.

Caregiver burden. Five indicators of responsibilities and burden associated with caregiving were examined. With one exception (noted below), they reflect 'primary' caregiver stressors, i.e. they relate to demands that directly arise from the caregiving situation (Pearlin *et al.* 1990; Pearlin, 1994). Firstly, caregivers indicated which of 10 household management duties they performed for the recipient (e.g. housework, running errands, providing transportation, money management; all items on this caregiver measure and those below are available from M.A.D.). The sum of endorsed items was calculated. Secondly, caregivers indicated which of 10 personal care and nursing tasks they performed for the recipient (e.g. assisting him/her to take medications, helping with walking, helping with bathing). The sum of endorsed items was determined. Thirdly, caregivers rated nine items concerning the degree to which their transplant-related caregiving responsibilities had affected the amount of time they had for other domains of their lives (e.g. personal affairs, recreational or vacation activities; adapted from Montgomery *et al.* 1985). The items were averaged, with higher scores indicating restricted time for the domains as a result of caregiving

(Cronbach's $\alpha=0.86$ for our sample). This time burden variable is considered in the Pearlin *et al.* (1990) conceptualization of caregiver stressors to reflect a 'secondary' stressor (i.e. one that is triggered by primary caregiving stressors). These three caregiver-reported measures had skewed distributions; respondents were classified as showing high levels of burden on a given measure if they scored in the upper third of the distribution.

The fourth measure of burden pertained to the physical functional status of the recipient early post-transplant, measured using the physical health subscales from the Sickness Impact Profile (SIP; Bergner *et al.* 1981). This information was obtained directly from the transplant recipient. The physical health subscales (totaling 52 items) assess the areas of sleep and rest, body care and movement, mobility, and ambulation. The percentage of items endorsed (each of which indicates presence of dysfunction) was determined. Individuals were classified as showing impairment if 20% or more of the items were endorsed; one third of the sample scored above this cut-point. In the absence of any clinically defined cut-point as to what constitutes serious impairment on the SIP subscales (De Bruin *et al.* 1992), we chose this cut-point based on empirical evidence that a level of 20% or higher is relatively rare across the many chronic illness samples for which descriptive data are available: less than one quarter to one tenth of respondents in a variety of samples have endorsed 20% or more of the physical subscales' items (Bergner *et al.* 1981; De Bruin *et al.* 1992). Finally, we evaluated the overall cognitive functioning of the recipient using the Mini Mental Status Examination (MMSE; Folstein *et al.* 1975). The MMSE includes 1–2 items to assess each of the areas of orientation to time and place, registration, attention, recall, ability to name, ability to follow verbal and written commands, and ability to copy a figure. Heart recipients scoring 25 or less were considered to fall in the impaired range on this measure, consistent with normative data on cut-points for this instrument (Folstein *et al.* 1975; Malloy *et al.* 1997).

Social supports and coping styles. Two areas of social supports available to the caregiver were assessed at the initial interview. The quality of

a respondent's relationship with the transplant recipient was measured with a 20-item questionnaire adapted from measures developed by Spanier (1976) and Pearlin & Schooler (1978), and used in various community-based and patient populations (Dew *et al.* 1997a, 2001). Items asked about the quality of multiple aspects of the relationship [e.g. 'how often does (the transplant recipient) show affection to you?', 'How often do you find yourself thinking over problems in your relationship?' 'Do you bring out the best in (the transplant recipient)?']. Principal-components analysis indicated that all items loaded on a single underlying factor; we thus created a summary measure for each caregiver by averaging the items (Cronbach's $\alpha=0.91$ for the present sample; 1=poor relationship; 5=excellent relationship). Support from friends was assessed with 14 items developed by Moos (1975) concerning the degree to which respondents felt they could rely on friends for emotional support (e.g. 'My friends make me feel that I'm a special person to them') and practical support ('My friends go out of their way to help me'). Based on a principal-components analysis, the items were averaged to form a summary index ($\alpha=0.88$ for the present sample; 0=poor support from friends; 3=excellent support from friends). The two social support measures had skewed distributions; scores were dichotomized at each variable's median into lower and higher support groups.

Four indices of coping style were examined. The 7-item Sense of Mastery Scale (Pearlin & Schooler, 1978) assessed the degree to which individuals felt in control of things that happened to them (e.g. 'I often feel helpless in dealing with the problems of life'; $\alpha=0.79$ for our sample; 1=low sense of mastery, 4=high sense of mastery). Additional indexes of coping style were derived from the Coping Checklist (Billings & Moos, 1981). On this measure, respondents are asked about the strategies they use in the context of a particular stressor – here, coping with what they considered to be the heart recipient's most serious health problem since initial hospital discharge post-transplant. This checklist yields three measures: active behavioral coping is the sum of positive responses to six questions (e.g. 'consulted a health professional'). Active cognitive coping is the sum of

positive responses to eight questions (e.g. 'drew on past experiences'). Avoidance coping is the sum of six questions (e.g. 'slept more to reduce feelings of tension'). The distributions of responses on these indexes were skewed; respondents were therefore classified as low users of a given coping strategy if they scored in the lower third of the distribution.

With one exception, the potential risk factors that we examined were themselves not highly intercorrelated (median=0.08, interquartile range=0.03–0.14); this indicates that they were tapping relatively independent areas. The exception was that caregivers who were men were more likely to be spouses of the heart recipients ($r=0.57$).

Analysis

Survival analysis, using a life-table approach (Cox & Oakes, 1984), was adopted as the key analytical strategy so that all available data were included from each individual until the end of the observation period or until their data were censored (due to either death or refusal). (We used a life-table approach rather than estimating Kaplan–Meier survival curves because, by the design of this clinical epidemiological study, individuals were retrospectively reporting on episodes occurring at any time since their previous interview. This is unlike the situation in clinical trials in which individuals are monitored daily or weekly and the exact date of episode onset can be determined very precisely.)

With the exception of PTSD-T, the cumulative percentages of the sample who developed each of the assessed psychiatric disorders post-transplant were calculated across five assessment intervals (0–2 months, 3–7 months, 8–12 months, 13–24 months, and 25–36 months post-transplant). For PTSD-T, the cumulative percentages were calculated across only two intervals during the first year post-transplant (0–7 months, 8–12 months), rather than three, since it was not assessed until the 12-month interview (see Instruments description above). Clinical features of all episodes of disorders occurring post-transplant (incident as well as recurrent) are also described.

The effects of potential risk factors on time to occurrence of two specific post-transplant

Table 2. Cumulative rates of onset (percentages and s.e.s) of selected DSM-III-R disorders during 36 months post-transplant in 190 caregivers

	Months post-transplant				
	2	7	12	24*	36*
Major Depression	16.8 (2.8)	23.1 (3.2)	23.8 (3.3)	25.4 (3.4)	31.6 (4.3)
Adjustment disorder, all types	17.7 (2.8)	26.2 (3.3)	28.4 (3.5)	29.2 (3.5)	35.4 (4.4)
With anxious mood	14.5 (2.6)†	23.2 (3.2)‡	25.4 (3.4)‡	26.2 (3.4)	29.4 (4.1)‡
With depressed mood	3.3 (1.3)	3.3 (1.3)	4.1 (1.5)	4.9 (1.7)	8.0 (2.7)
Transplant-related Post-Traumatic Stress Disorder§	—	17.0 (3.0)	19.3 (3.2)	20.9 (3.3)	22.5 (3.6)
GAD	—	2.5 (1.2)	3.2 (1.4)	4.1 (1.6)	7.3 (2.7)
Any of the above disorders post-transplant	28.6 (3.4)	45.2 (3.8)	47.2 (3.8)	48.8 (3.9)	56.3 (4.5)

* At 36 months post-transplant, disorders were assessed and were retrospectively dated at that time to have onset occurring during the second or third year post-transplant.

† Includes 2 cases of Adjustment disorder with mixed anxiety and depression.

‡ Includes 1 cases of Adjustment disorder with mixed anxiety and depression.

§ Initially assessed at 12 months post-transplant and retrospectively dated at that time to have its onset occurring from 0–7 months post-transplant or 8–12 months post-transplant.

psychiatric outcomes (first onset of MDD; first onset of any of the anxiety disorders) was evaluated in the context of survival analysis. Individual as well as combined effects of the risk factors were considered.

RESULTS

Cumulative prevalence rates post-transplant

Table 2 presents the cumulative risk for onset of the targeted DSM-III-R disorders in the cohort across the first 36 months post-transplant. By 36 months post-transplant, 31.6% of the cohort had experienced MDD. MDD was more likely to first occur during the first 12 months post-transplant than in subsequent months, although the cumulative prevalence continued to increase – albeit at a slower rate – throughout the study period. A similar pattern appeared for Adjustment disorder with depressed mood and Adjustment disorder with anxiety.

By contrast, Table 2 shows that the great majority of cases of PTSD-T occurred during the first 12 months post-transplant, with very little increase thereafter. Most cases occurred in the earliest months after the transplant and thus were, by DSM definition, cases with immediate (rather than delayed) onset. GAD, on the other hand, showed a steady, linear increase in cumulative prevalence rate across the entire 36-month period. Overall, the 12-month cumulative prevalence rate of any of the assessed

disorders post-transplant was 47.2%; the cumulative prevalence rose to 56.3% by 36 months post-transplant.

Characteristics of post-transplant psychiatric episodes

Table 3 summarizes characteristics of caregivers' episodes of MDD and anxiety disorder (Adjustment disorder with anxiety, GAD), classified by whether the episodes occurred earlier *versus* later post-transplant. (PTSD-T episodes could not be so classified since all but three episodes began during the first year post-transplant.) The table includes descriptive information on all episodes occurring during the 3-year study period regardless of whether they represented the initial onset of the disorder post-transplant (see third note to Table 3).

There were no reliable differences between earlier *versus* later episodes of MDD or anxiety disorder in terms of duration, the presence of functional impairment, whether professional help was sought, or whether caregivers received psychotropic medications. Overall, as shown Table 3, less than 50% of individuals sought professional help during their episodes, and even lower percentages were likely to have been prescribed psychotropic medications (primarily antidepressants). Although the most common precipitants for depression and anxiety in the early months post-transplant pertained directly to the transplant recipient's physical health,

Table 3. Clinical characteristics of all post-transplant episodes of DSM-III-R Major Depression and anxiety disorder (Adjustment disorder and Generalized Anxiety Disorder)*

	Total no. of cases	Time of episode post-transplant		χ^2 test	p^\dagger
		Early (≤ 7 months)	Late (8–36 months)		
Major Depression	$n = 66^\ddagger$	$n = 49$	$n = 17$		
Length of episode > 1 month, % yes	62.1	63.3	58.8	0.11	0.745
Median, weeks (range: 2–52 weeks)	4	4	4		
Functional impairment, % yes	80.0	81.3	76.5	0.18	0.729
Sought professional help, % yes	48.5	42.9	64.7	2.41	0.120
Prescribed psychotropic medication, % yes	28.8	24.5	41.2	1.71	0.190
Event precipitating episode§					
% transplant-related physical health	48.4	61.2	29.4	5.32	0.074
% transplant-related psychosocial	31.3	26.5	52.9		
% other	20.3	12.2	17.6		
Anxiety disorder	$n = 69^\ddagger$	$n = 49$	$n = 20$		
Length of episode > 1 month, % yes	85.5	87.8	80.0	0.69	0.460
Median, weeks (range: 2–164 weeks)	4	4	5		
Functional impairment, % yes	74.2	69.6	85.0	1.74	0.188
Sought professional help, % yes	43.5	40.8	50.0	0.49	0.485
Prescribed psychotropic medication, % yes	21.7	24.5	15.0	—	0.526
Event precipitating episode§					
% transplant-related physical health	50.0	64.6	20.0	12.15	0.002
% transplant-related psychosocial	27.9	27.1	50.0		
% other	22.1	8.3	30.0		

* See text for description of clinical characteristics of PTSD-T.

† Fisher exact test p values are reported for variables with minimum expected cell frequencies less than 5.

‡ Forty-seven persons had 66 episodes of Major Depression, and 51 persons had 69 episodes of anxiety disorder. For any given characteristic, its correlation within the same individual over time was small and no stronger than its correlation across pairs of separate individuals. Therefore, all episodes were entered as independent units in the comparisons of early *versus* late episodes.

§ Respondents' descriptions of events precipitating episodes of disorder were coded as related to (a) the transplant recipient's physical health if any physical aspect of the transplant experience was noted (e.g. occurrence of rejection; infections), (b) psychosocial aspects of the transplant if they could not be directly ascribed to the recipient's physical health (e.g. problems paying hospital bills; having to change residence because of the transplant) or (c) other non-transplant-related events if they could not be directly linked to the transplant (e.g. events at the caregiver's job; other family members diagnosed with an illness).

greater proportions of the later episodes were reported to have been triggered by psychosocial sequelae of the recipient's transplant (e.g. financial problems related to long-term medical care needs) or non-transplant-related events and circumstances.

PTSD-T occurred almost exclusively early post-transplant, and we have described this disorder in caregivers during this time period previously (Stukas *et al.* 1999). We note here that the median duration was 28 weeks (interquartile range, 9–52 weeks). Only 21% of caregivers sought professional mental-health treatment, and 9% had received medications. The period of waiting for a donor heart was the most commonly cited aspect (33%) of the transplant experience that provoked post-transplant reactions, followed by learning about the recipient's need for a transplant (15%), and the initial evaluation for transplant (27%).

Risk factors for psychiatric disorder post-transplant

In order to examine which factors before and shortly post-transplant increased caregivers' risk of psychiatric disorder, we focused on two outcomes: the occurrence of MDD, and the occurrence of any anxiety disorder (Adjustment disorder with anxiety, GAD, PTSD) across the 3-year post-transplant period.

The left-hand side of Table 4 shows the categories of potential risk factors that were considered, including historical, pre-transplant characteristics (demographic and psychiatric history variables) and early post-transplant caregiver burden and social support and coping variables. The first column of Table 4 displays the sample distribution on each of these risk factors, e.g. 71 persons in the cohort (37.4%) had a positive history of depressive or

Table 4. Tests of differences in time to onset of post-transplant psychiatric disorder and cumulative proportions of family caregivers who experienced psychiatric disorders according to hypothesized risk factors

Potential risk factor	n†	Cumulative risk of disorder by 36 months post-transplant			
		Major Depression		Anxiety disorders	
		Test comparing survival curves	Cumulative proportion (S.E.)	Test comparing survival curves	Cumulative proportion (S.E.)
Background factors					
History of depression or anxiety					
Yes	71	28.06***	0.57 (0.08)	19.50**	0.63 (0.07)
No	119		0.15 (0.04)		0.28 (0.05)
Gender					
Female	162	1.98	0.34 (0.05)	1.95	0.43 (0.05)
Male	28		0.12 (0.06)		0.34 (0.14)
Age					
≤ 50	104	0.44	0.31 (0.05)	3.73*	0.49 (0.06)
> 50	86		0.32 (0.07)		0.33 (0.06)
Education					
≤ high school	113	1.02	0.37 (0.06)	0.80	0.50 (0.06)
> high school	76		0.24 (0.06)		0.31 (0.06)
Caregiver employed					
Yes	107	3.67*	0.25 (0.05)	0.04	0.43 (0.06)
No	82		0.40 (0.07)		0.40 (0.06)
Relation to recipient					
Spouse	137	2.78	0.36 (0.05)	3.23	0.45 (0.05)
Other	53		0.17 (0.06)		0.31 (0.09)
Caregiver burden					
Household tasks					
More	60	15.62***	0.50 (0.08)	11.92**	0.60 (0.07)
Fewer	126		0.22 (0.05)		0.32 (0.05)
Nursing care tasks					
More	75	3.70*	0.39 (0.07)	8.84**	0.54 (0.07)
Fewer	111		0.27 (0.06)		0.32 (0.06)
Restrictions on personal time					
More	61	2.20	0.23 (0.07)	7.20**	0.29 (0.08)
Fewer	126		0.35 (0.05)		0.48 (0.05)
Recipient had physical functional limitations by 2 months post-transplant					
Yes	56	0.82	0.37 (0.09)	0.68	0.48 (0.08)
No	130		0.29 (0.05)		0.40 (0.05)
Recipient had cognitive impairment					
Yes	26	0.85	0.16 (0.08)	1.38	0.36 (0.13)
No	154		0.34 (0.05)		0.42 (0.05)
Social supports and coping					
Poor relationship with recipient					
Yes	61	9.96**	0.42 (0.08)	15.65***	0.61 (0.08)
No	125		0.25 (0.05)		0.32 (0.05)
Low support from friends					
Yes	64	2.74	0.40 (0.08)	1.39	0.52 (0.08)
No	122		0.27 (0.05)		0.37 (0.05)
Low sense of mastery					
Yes	72	3.02	0.37 (0.07)	8.75**	0.62 (0.07)
No	112		0.29 (0.06)		0.28 (0.05)
Low use of active cognitive coping					
Yes	68	0.50	0.29 (0.07)	0.42	0.42 (0.07)
No	104		0.33 (0.06)		0.45 (0.06)
Low use of active behavioral coping					
Yes	74	1.33	0.35 (0.07)	0.004	0.44 (0.07)
No	98		0.29 (0.06)		0.44 (0.06)
High use of avoidance coping					
Yes	53	0.09	0.32 (0.08)	5.26*	0.61 (0.09)
No	119		0.32 (0.05)		0.36 (0.05)

† Values on each variable sum to less than 190 when respondents were missing data on the variable.

‡ Wilcoxon test statistic from survival analysis with 1 df.

* $p \leq 0.05$, ** $p < 0.01$, *** $p < 0.001$.

anxiety-related disorders prior to transplant, the remainder did not.

A series of separate survival analyses were conducted for each of the two psychiatric outcome variables, in which individuals with and without each risk factor were compared to determine whether they differed in time to post-transplant onset of disorder across the 36-month study period. Results are displayed in Table 4. Firstly, as shown in the second and fourth columns of Table 4, persons with a prior psychiatric history had significantly shorter times to onset of MDD [Wilcoxon test of difference in survival curves for those with *versus* without a psychiatric history ($df = 1$) = 28.06, $p < 0.001$], as well as onset of anxiety disorders [Wilcoxon test ($df = 1$) = 19.50, $p < 0.01$]. Table 4 also presents the cumulative proportions of each risk factor group who met criteria for MDD or for any anxiety disorder by the end of the 36-month follow-up period post-transplant; for example, 57% of those with a positive history had episodes of MDD post-transplant, compared to 15% of individuals without a pre-transplant history. Additional factors that increased the cumulative likelihood of both MDD and anxiety disorders include greater caregiver burden related to household and nursing tasks, and having a poor relationship with the heart recipient. Lack of caregiver employment outside of the home increased risk for MDD. Several additional factors increased the risk for anxiety disorders, including younger age, greater restrictions on personal time imposed by caregiver responsibilities, a low sense of personal mastery, and high use of avoidance strategies for coping with the health problems of the recipient.

Given the importance of pre-transplant psychiatric history, caregiver burden from household and nursing tasks, and the quality of the relationship with the heart recipient for both categories of post-transplant psychiatric outcome variables, additional survival analyses were performed to determine whether each of these risk factors interacted with – or modified – each other and/or any of the other potential risk factors' effects. There was no statistically reliable evidence of any such effects (results available from M.A.D.). In other words, the impact of the factors appeared to be additive. Two illustrative examples of the additive nature of the effects are shown in Fig. 1. Fig. 1a displays

cumulative onset curves for MDD, with the study sample grouped according to level of caregiver burden related to household tasks and quality of the relationship with the heart recipient.[†] Respondents with both risk factors were most likely to experience MDD, followed by individuals with just one of the risk factors. Respondents with neither factor were least likely to develop MDD post-transplant. Fig. 1b provides a similar illustration of risk factors' additive effects on anxiety disorders, displaying respondents grouped according to caregiver burden related to household tasks and caregivers' perceptions of personal mastery.

Since risk factors' effects appeared additive, we performed a final survival analysis to examine whether the total number of risk factors that respondents possessed significantly increased their risk for onset of MDD post-transplant and, similarly, whether total risk-factor count increased the risk of anxiety disorders. For each of these two outcomes, we created a 'dose' variable by determining how many risk factors each respondent possessed, and the risk factors were those found individually to be significantly associated with time to onset of psychiatric disorder post-transplant. For MDD, these included a positive psychiatric history, lack of employment, caregiver burden related to household tasks, burden related to nursing tasks, and a poor relationship with the heart recipient. For anxiety disorders, these included a positive psychiatric history, age, household task burden, nursing task burden, restrictions on personal time due to caregiving, a poor relationship with the recipient, a low sense of mastery, and high use of avoidance coping strategies.

For MDD, results indicated that by 36 months post-transplant, only 13% of caregivers

[†] It is important to note that the curves drawn in the figure follow the traditional graphical presentation of life-table data in which the increase in cumulative rate of onset appears as a 'stair-step' function rather than as a gradual increase over time (Cox & Oakes, 1984). Each 'step' reflects the total rate of onset during a given period of observation. For example, at the 2-month assessment, the rate of MDD for the sample as a whole totaled 16.8%. These episodes could have begun at any point between 0 and 2 months post-transplant. Thus, the figures should not be mistakenly interpreted to mean that there were no episodes of MDD until the moment of the 2-month assessment. On the contrary, some episodes began simultaneously with the patient's transplant. As noted in the Methods section, a life-table approach was more appropriate for our retrospectively reported data than a Kaplan-Meier approach to estimating the cumulative onset curves.

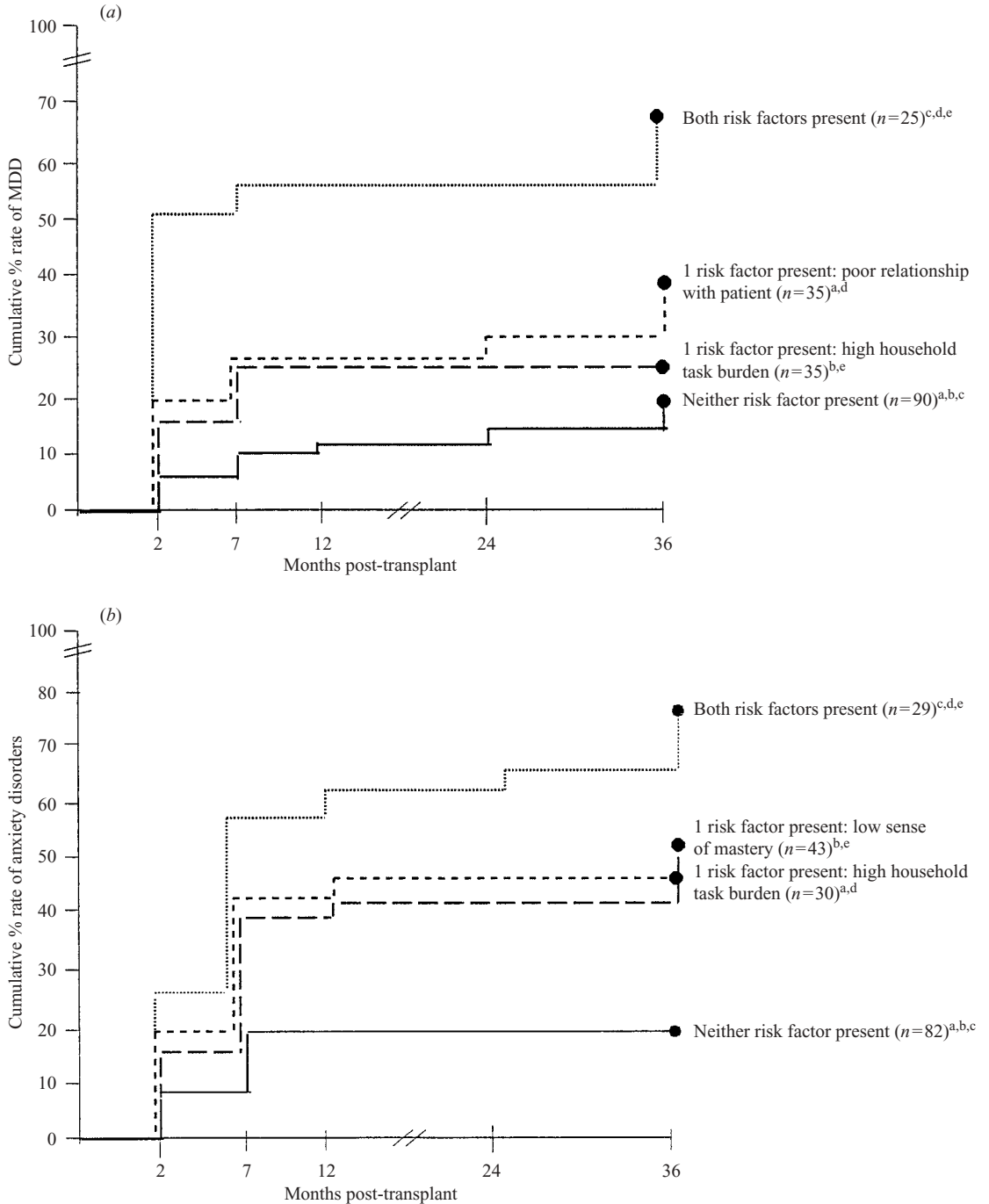


FIG. 1. Examples of additive effects of individual risk factors on time to onset of MDD or anxiety disorder post-transplant. Survival curves with identical superscripts indicate pairs of groups differing at $p < 0.05$. (a) Effects of caregiver household task burden and poor relationship with heart recipient on risk for MDD [test of overall differences between survival curves, Wilcoxon test (3) = 25.94, $p < 0.0001$]. (b) Effect of caregiver task burden and low sense of mastery on risk for anxiety disorders [test of overall differences between survival curves, Wilcoxon test (3) = 27.04, $p < 0.0001$].

with 0–1 risk factors had experienced any episodes of MDD. In contrast, 32% of caregivers with 2 risk factors, 52% of those with 3 risk factors, 52% with 4 risk factors, and 90% of those with all 5 risk factors had episodes of MDD by the end of the follow-up period [Wilcoxon test ($df=4$)=39.40, $p<0.0001$]. Similar results were obtained for anxiety disorders. By 36 months post-transplant, 4% of caregivers with 0–1 risk factors had experienced anxiety disorders; 21, 40, 57 and 83% of those with 2, 3, 4 and 5 or more risk factors respectively, had episodes of anxiety disorders by the end of the follow-up period [Wilcoxon test ($df=4$)=42.80, $p<0.0001$].

DISCUSSION

Over 272 000 organs, including over 31 500 hearts, have been transplanted in the United States alone in the last 15 years (OPTN, 2002). In the case of heart transplantation, the use of permanent ‘artificial hearts’ (mechanical circulatory support systems) is increasing and may eventually obviate the need to rely on the limited pool of available human donor hearts. Thus, the population of patients who receive new hearts may grow at an increased rate in coming years (Goldstein *et al.* 1998). The corresponding rise in the numbers of family caregivers who provide long-term support and assistance to these patients will necessitate greater focus on these caregivers’ needs and well-being.

Our study is the first to provide information regarding rates, timing of onset, and key risk factors for diagnosable depression and anxiety-related disorders in caregivers across the first several years after their family member’s transplant. Over 50% of these caregivers met criteria for one or more of the disorders assessed, with MDD, Adjustment disorders, and PTSD-T being particularly common. Although direct comparisons to other caregiver cohorts are difficult due to differences in definitions of clinically significant distress and differences in time periods for which rates are reported, the level of disorder in our sample appears similar to or greater in magnitude than that observed in other caregiver studies. In the largest investigation to date, in which a sample of 1219 family caregivers to persons with chronic illness was

surveyed, the total rate of any mood or anxiety disorder during the past year was 21%. Six per cent met criteria for mood disorder (MDD, dysthymia, or bipolar illness) and 17.5% met criteria for anxiety disorders (GAD, phobias, or panic disorder) (Cochrane *et al.* 1997). Our rates during the first 12 months post-transplant well exceed these rates. Other studies examining prevalence rates over 2- to 3-year periods, primarily in caregivers to dementia patients, report rates that are similar in magnitude to our cumulative 3-year rates of onset (e.g. Gallagher *et al.* 1989; Schulz *et al.* 1995).

The disorder rates in our caregiver sample are greater than the cumulative onset rates that we have previously reported in the transplant recipients to whom they provided care (Stukas *et al.* 1999; Dew *et al.* 2001). By 3 years post-transplant, 38% of the heart recipients themselves had experienced one or more depressive or anxiety disorders, with 25% meeting criteria for MDD and 17% meeting criteria for PTSD-T; there was only one case of GAD. The present rates for their caregivers are 1.2–5 times larger. A similar excess in rates among caregivers relative to patients was noted in a report of the burden of living with amyotrophic lateral sclerosis (Rabkin *et al.* 2000). Such findings attest to the need to consider caregiver distress when evaluating the impact of a patient’s illness. However, as is typical in most psychiatric and community-based studies (Cochrane *et al.* 1997; Katz *et al.* 1997), only a minority of our sample sought professional help or received psychotropic medications, despite the facts that their distress may have lasted for many weeks or months and was usually associated with functional impairment in home and work domains.

With regard to the timing of initial onset of post-transplant psychiatric disorders, data from the present sample, as well as other reports examining subclinical distress levels in transplant caregivers, clearly indicate that the first year following the transplant surgery is a period of elevated risk for many of the disorders that we examined. In particular, almost all new onsets of PTSD-T occurred during the first year. This disorder, with its hallmarks of flashback experiences and heightened arousal associated with reminders of events surrounding the transplant, appears to represent a failure of the individual to come to terms with the acute

stressors of the transplant experience (Dew *et al.* 1999; Stukas *et al.* 1999). In contrast, the types of disorders typically associated with chronic stressor exposure, including MDD and GAD (Baum *et al.* 1999; Dohrenwend, 2000) showed slower, steadier increases over the entire time period in our caregiver sample. This continuing cumulation of new episodes of these disorders is consistent with the long-term nature of the transplant experience, in which acute stressors surrounding the initial surgery and perioperative recovery evolve into a constellation of ongoing, chronic stressors related to additional health complications and the psychosocial status of the transplant recipient (Dew *et al.* 2002). Our findings that the precipitants of depressive and non-PTSD anxiety disorders appeared to shift away from direct, transplant-related physical health issues in the early months post-transplant to psychosocial sequelae of living with the transplant also support a chronic stressor interpretation of caregivers' continuing risk for these disorders.

A third piece of evidence further supports the chronic stressor perspective. As noted earlier, we decided to conduct the final 36-month follow-up assessment because the third year post-transplant often marks the beginning of the manifestation of significant long-term post-transplant complications such as cardiac allograft disease and cancers that are attributable not to the transplant surgery *per se* but to factors such as the immunosuppressant regimen and the transplant recipient's 'life-style' behaviors (e.g. weight gain and obesity, resumption of smoking). Consistent with the increased risk of these complications, there is an apparent trend in the onset data in Table 2 showing a somewhat increased rate of cases of caregiver psychiatric disorders during this third year (25–36 months post-transplant) compared to the rate of new cases observed during the 13- to 24-month period. While our sample of cases in the present study is too small to investigate this trend more systematically in relation to other factors, it further suggests the importance of carefully considering timing of episode onset in caregiver samples such as ours. It is possible that the increase in case rate during the final observation period may have been due to a 'forward telescoping' of respondents' memory for episodes that occurred closer to the actual

time-point of assessment (i.e. at 36 months post-transplant). However, we feel that (a) our use of strategies to facilitate accurate dating of episodes and (b) the fact that the 24 months of recall covered in the final assessment was relatively brief, both limited the impact of this potential bias. With regard to the latter, it has been found in previous community-based retrospective studies of up to 15–20 years that the bias is least when the period of retrospective recall is as short as the 24 months covered by our final assessment (Lyketsos *et al.* 1994; Eaton, 1995).

Although the cumulative rates of disorders in our sample were high, many caregivers did not develop significant depression or anxiety in the years after their family member's transplant. Several pre- and early post-transplant characteristics were important predictors of caregivers' mental health outcomes, and we also found that the sheer number of such characteristics that caregivers possessed influenced whether they would experience a post-transplant psychiatric disorder. In addition to the powerful impact of prior psychiatric history on risk, elements of caregiver burden were among the most critical predictors of risk for both MDD and the anxiety disorders that we examined. Objective, 'primary' elements of burden, pertaining to numbers of household and nursing care tasks (and, in the case of anxiety, the 'secondary' burden of increased time constraints due to caregiving) significantly increased risk for disorder. Interestingly, the actual physical functional or cognitive status of the recipient did not affect risk. Task performance has been described as one of the most salient components of transplant caregiver burden, with a greater potential to lead to life-style changes than that resulting from other common elements of burden such as worry about the recipient's health or financial difficulties (Hyler *et al.* 1985; Dew *et al.* 2000). While greater task burden has been found to negatively affect both the transplant caregiver's physical health and social functioning (Mishel & Murdaugh, 1987; Grundböck *et al.* 1992; Dew *et al.* 1998*a*), its impact on mental health has received previous consideration only in the context of subclinical psychiatric distress (Canning *et al.* 1996).

One of the background characteristics that we considered (caregivers' employment status)

might also be conceptualized as indirect measure of caregivers' burden, although previous research has found the direction of its effect on mental health to vary. Thus, while holding a job outside the home might serve as a caregiver stressor and lead to poorer mental-health outcomes, caregiver employment has also been found to be associated with improved mental health, perhaps through its capacity to provide additional social and financial supports and/or a respite from caregiving responsibilities (Martire *et al.* 1997; Edwards *et al.* 2002). Our findings regarding risk for depression support the latter view.

Beyond background and caregiving burden characteristics, we examined other psychosocial resources that might affect caregivers' risk for psychiatric disorder. By far the most influential was the quality of their relationship with the heart recipient. A strong relationship with the patient has repeatedly been found to be a critical factor in predicting distress in individuals engaged in a variety of caregiving roles (Schulz *et al.* 1990, 1995; Eisdorfer, 1991). This appears to extend to transplant family caregivers as well.

In contrast, effects of remaining psychosocial factors that we assessed were less striking. Neither support from friends nor coping style or strategies influenced caregivers' risk for MDD. However, a lower sense of personal mastery or competence, as well as greater use of avoidance strategies for coping with the transplant recipient's ongoing health problems led to increased risk for anxiety disorders in the caregivers. Finally, the fact that younger caregivers were also at higher risk for anxiety may indirectly reflect a less developed repertoire for coping with post-transplant burden and stressors.

There are several limitations of the current work. Firstly, we have already discussed possible bias in dating the onsets of psychiatric disorders that arise when respondents are reporting retrospectively on specific periods of time. We were able to complete clinical reassessments at relatively closely spaced time-points during the first year post-transplant, and we took steps to facilitate accurate dating over the period 13–36 months post-transplant. Secondly, the majority of our caregivers were women. Given that female gender is a known risk factor for depression and anxiety, the fact that disorder

rates were higher in these caregivers than in heart recipients themselves is undoubtedly due in part to the fact that most heart recipients are men. However, as noted above, the elevated caregiver rates are also consistent with rates reported in the extensive literature on caregiver distress. Thirdly, the correlational nature of our results – although strengthened by the longitudinal design – precludes etiological interpretations of predictor–outcome associations. In addition, it might be suggested that collecting 'baseline' pre-transplant information on, for example, caregivers' psychiatric history or relationship with the patient would have further clarified the interpretation of any associations. Unfortunately, data collected pre-transplant while patients are waiting on the transplant candidate list is not truly baseline since it is biased by the strain of uncertainty and by the fears of patients and their families that any negative information they provide may endanger their chances for transplantation. With respect to the patient–caregiver relationship, family members often undergo dramatic temporary role changes during the waiting period, they may need to relocate their households to be nearer to the transplant center, or they may spend long periods separated from the patient in the event of hospitalization. These elements ensure that the pre-transplant period will provide an unsatisfactory benchmark as to pre-existing relationship quality. Instead, therefore, our primary interest focused on post-transplant relationships, burden, and psychosocial status, and we thus began data collection after patients returned home post-transplant, coupled with a retrospective assessment of pre-transplant psychiatric history.

Finally, with respect to pre-transplant psychiatric history in particular, its role as a strong predictor of post-transplant mental-health outcomes might have been delineated in a more fine-grained manner if we had separately examined caregivers' history of disorder before they entered the caregiving role, during their family member's illness and associated caregiving, and/or during the most debilitating period of the illness (i.e. while the patient was on the waiting list for the transplant) (Dura *et al.* 1990). Our assessments did attempt to distinguish onsets of caregiver disorder earlier in their lifetimes *versus* after their family member was placed on the

transplant waiting list. However, it was not possible to separately examine the impact of disorder occurring in these two separate pre-transplant time periods, in large part because of the already-high rates of lifetime disorder by the time the patient's illness reached its worst. It is also difficult with an often slow, insidious illness like heart disease to precisely date a moment of onset of the caregiving role so that we could have inquired about psychiatric disorder before and after caregiving began. We did not feel that our psychiatric interviews were capable of this level of precision on a retrospective basis. In sum, our crude measure of pre-transplant psychiatric history – given its important predictive effects on post-transplant outcomes – deserves more careful consideration in the future, including the continued development of strategies to facilitate retrospective reports over extended time periods involving events with insidious as opposed to clear-cut onsets and offsets.

Future studies must expand beyond the set of potential predictor variables that we were able to examine to consider other characteristics as well. For example, stable personality characteristics may affect caregiver mental health (Hooker et al. 1992; Bookwala & Schulz, 1998). Moreover, the specific course of the transplant recipient's health over time post-transplant, as well as other elements of the caregiver's own physical health that change over the post-transplant years may have reciprocal effects on the caregiver's emotional well-being (Dew et al. 1998a; Shewchuk et al. 1998). However, from the standpoint of intervention development, a focus on the psychosocial assets and liabilities that patients and their family caregivers possess early post-transplant – after the strain of the waiting period and the surgery but before any long-term complications arise – may be the most realistic strategy for the true prevention of caregiver mental-health problems in the face of post-transplant stressors. Prevention of caregiver psychiatric disorder may, in turn, help to maximize the quality of life of the transplant recipient.

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