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Psychological Factors in End-Stage Renal Disease: An Emerging Context for Behavioral Medicine Research

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End-stage renal disease (ESRD) is a chronic, life-threatening condition afflicting over 300,000 Americans. Patient nonadherence and psychological distress are highly prevalent among ESRD patients, and both have been found to contribute to greater morbidity and earlier mortality in this population. A range of factors have been examined as potential determinants of adherence and adjustment. Evidence suggests that adherence and adjustment are maximized when a patient's preferred style of coping is consistent with the contextual features or demands of the renal intervention the patient is undergoing. Challenges for future clinical research include refining methodologies for the assessment of depression and adherence, more clearly evaluating the efficacy of psychological interventions, and clarifying the role that depression and social support play in influencing patient mortality.

The over 300,000 end-stage renal disease (ESRD) patients in the United States face an incurable, life-threatening, chronic disease. Only four decades ago, an ESRD diagnosis meant near certain death. Upon the cessation of renal function, excess fluid, metabolic toxins, and electrolytes rapidly accumulate in blood and bodily tissues. These substances must be removed by alternative means if the ESRD patient is to survive. For most patients, ESRD is the end result of a progressive deterioration in kidney function over a period of months or years that is secondary to another chronic medical condition (e.g., diabetes or hypertension). Diabetic nephropathy is the most common etiological factor, accounting for over one third of new ESRD cases (U.S. Renal Data System [USRDS], 1999).

Currently available treatments for ESRD include renal transplantation and several forms of renal dialysis. In general, the choice of a particular ESRD treatment is substantially influenced by nonmedical factors, including patient and provider preferences and judgments about which modality is likely to be associated with the most favorable patient adherence and quality of life (Christensen & Moran, 1998; Davison, 1996). A successful renal transplant is generally thought to hold certain advantages in terms of patient quality of life (Christensen, Holman, Turner, Smith, & Grant, 1991). However, because of a perennial shortage of donor organs and a significant transplant rejection rate, renal dialysis remains the prescribed treatment for the large majority of patients.

There is an important difference in the degree of patient involvement in the delivery of the different forms of dialysis. The center hemodialysis patient is a relatively passive recipient of a treatment that is carried out in a hospital or clinic. The hemodialysis procedure is performed three times a week by nurses or technicians with each session lasting approximately 4 hours. Hemodialysis treatment involves a vascular connection made between the artificial kidney (dialyzer) and the patient, usually through an arteriovenous fistula permanently placed in the patient's forearm. Nurses or technicians are responsible for directing each step in the initiation, monitoring, and discontinuation of each dialysis session. Little participation is required or allowed of the patient during treatment delivery.

For some patients, hemodialysis is carried out at home. Although home and center hemodialysis are largely analogous from a physiological and mechanical standpoint, home patients have the opportunity to be much more actively involved in treatment delivery and direction. Moreover, home dialysis patients have considerably less frequent contact with renal care providers and are able to set and maintain their own dialysis schedules.

Peritoneal dialysis treatment typically requires the patient to take an even more active role in treatment delivery. In continuous ambulatory peritoneal dialysis (CAPD), the most common form of peritoneal dialysis, a permanent catheter is surgically implanted in the abdomen. A sterile tube is used to connect the catheter to a bag of sterile dialysis solution (dialysate). The bag is elevated to allow flow of the dialysate into the peritoneal cavity. After this procedure is completed, the bag is tucked away under the patient's clothing. Over the next 4 to 8 hr, the patient remains ambulatory as blood filters through the peritoneal membrane, leaving toxins and excess fluid behind in the dialysate. After this phase of the procedure is complete, the bag is lowered and the used solution is drained back into the bag, where it is discarded and the dialysate exchange procedure begins again.

In the late 1960s renal transplantation became another viable treatment option for the ESRD patient. Approximately 28% of ESRD patients currently have a functioning kidney transplant (USRDS, 1999). Renal grafts come from either a cadaveric (brain dead) or living (typically a first-degree relative) donor. For most patients, the renal transplantation experience involves a transition toward greater independence from health care providers. Transplant patients are responsible for the management of their immu-

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nosuppressive regimen, having regular laboratory work done at a laboratory or clinic near their home, and monitoring themselves for early signs of organ rejection or infection. Direct contact between postrenal transplant patients and care providers is usually less frequent than the intensive and frequent contact between center hemodialysis patients and their renal care providers.

Despite recent advances in immunosuppressive therapy, activation of the patient's immune system resulting in organ rejection and potential graft failure remains an important limitation to the potential benefit of transplantation. Approximately 40% of cadaveric renal graft recipients experience a clinically significant acute rejection episode in the first year following transplant (Johnson et al., 1997). Most acute rejections are successfully reversed, as only 10%–15% of cadaveric transplants actually fail in the first year (USRDS, 1999). Despite higher success rates for living related donation, approximately 70% of renal transplants involve cadaveric donors (USRDS, 1999).

Psychological Factors in ESRD

In many ways, ESRD is unique among medical conditions. The extreme dependence on artificial means for survival and the substantial behavioral demands placed on the patient have few parallels in health care. Despite the uniqueness of the disorder, most of the central clinical issues and problems observed in this population are also seen in other chronic medical conditions. This article focuses primarily on three issues that have received considerable attention in the empirical literature on psychological factors in ESRD. These issues include patient nonadherence with the medical treatment regimen, patient emotional distress, and psychosocial influences on physical morbidity and mortality. We address several additional issues that have received less attention in the past but that we believe reflect areas in which behavioral medicine researchers and clinicians can make important contributions to the care and treatment of the ESRD patient.

Nature, Prevalence, and Implications of Dialysis Regimen Nonadherence

Perhaps the most important behavioral influence on ESRD patient outcomes involves adherence to the prescribed medical treatment regimen. In addition to undergoing frequent and time-consuming dialysis treatments, patients receiving all forms of ESRD treatment face a multifaceted behavioral regimen. For example, center and home hemodialysis patients face extreme restrictions on the amount of fluid that can be safely consumed. Prolonged fluid overload is associated with congestive heart failure, hypertension, pulmonary edema, and shortened patient survival (Wolcott, Maida, Diamond, & Nissenson, 1986).

Both peritoneal and hemodialysis patients are required to take regular doses of phosphate-binding medication as well as to reduce intake of phosphorus-rich foods because of the body's inability to excrete phosphorus while undergoing dialysis treatment. Sustained elevations in serum phosphorous (P) are associated with a variety of complications, including renal osteodystrophy, serious decreases in calcium, and subsequent bone demineralization. Serum P levels greater than 6.0 mg/dl are generally considered indicative of problematic adherence. Further dietary modification (i.e., restriction of potassium-rich foods) is necessary for patients to maintain safe serum potassium (K) levels. Hyperkalemia (i.e., serum K > 5.5 mEq/l) is a clinically significant problem for many dialysis patients owing to their body's inability to regulate potassium levels. If potassium intake guidelines are not followed, serum K will rise, and potentially life-threatening cardiac arrhythmia can occur.

As is the case with most medical populations, obtaining a valid and reliable assessment of adherence to the various facets of the renal dialysis treatment regimen presents a significant challenge to both researchers and clinicians. The most commonly used adherence criteria in the ESRD literature involve indirect biochemical or physiological markers of patient adherence. Although biochemical assessments have the advantage of being relatively unaffected by human judgments, such assessments are potentially confounded by nonbehavioral factors. For example, serum K is known to be influenced by factors other than patient dietary behavior (e.g., changes in the dialysis prescription, a variety of acute medical illnesses). In contrast, adherence to the fluid-intake restrictions among hemodialysis patients can be quite accurately determined by computing the amount of weight a patient gains between dialysis treatment sessions. The values resulting from this computation (termed *interdialytic weight gain*, or IWG) are believed to be a valid reflection of the amount of fluid the ESRD patient ingests between sessions (Manley & Sweeney, 1986). IWGs greater than 2.5 kg are typically considered indicative of problematic adherence. Maintaining IWGs at this level generally requires the patient to ingest no more than 1.0–1.5 L of fluid (including fluid in food) per 24-hr period.

Studies examining the prevalence of nonadherence among renal dialysis patients have typically observed that between 30% and 60% of dialysis patients do not adhere to diet, fluid-intake, and medication regimens (Bame, Petersen, & Wray, 1993; Christensen et al., 1992; Friend, Hatchett, Schneider, & Wadhwa, 1997; Moran, Christensen, & Lawton, 1997; Schneider, Friend, Whitaker, & Wadhwa, 1991). In general, past reports indicate that nonadherence is most common for fluid-intake restrictions and somewhat less common for dietary or medication guidelines.

Some investigations of adherence have focused on the dialysis treatment schedule itself (Kimmel et al., 1995; Kimmel, Peterson, et al., 1998). In these studies, adherence has been defined either as the percentage of attendance with the three-times-per-week hemodialysis schedule or as the amount of time a patient actually receives dialysis relative to the amount of dialysis time the physician had prescribed for a given 3–4-hr session. This method of defining adherence avoids many of the problems inherent in relying on indirect biochemical markers as reflections of behavior. However, missing a dialysis session altogether is a relatively rare occurrence. Kimmel, Peterson, et al. (1998) reported that in a study of 295 patients, on average, less than 2% of hemodialysis sessions were missed over a 3-month period. Moreover, the shortening of a treatment session may be confounded by factors such as symptoms or problems that occur during dialysis or differences in provider judgments or practice style.

Nonadherence Following Renal Transplantation

Patients receiving a renal transplant are largely free from the dietary and fluid-intake constraints posed by dialysis treatment. However, transplant patients are required to follow a strict immunosuppressive medication regimen, attend frequent clinic and laboratory appointments, and remain vigilant about physical changes that may signal organ rejection or infection. Patient nonadherence to the immunosuppressive regimen is believed to be an important contributor to renal graft rejection and failure (Armstrong & Weiner, 1981; De Geest et al., 1995; Didlake, Dreyfus, Kerman, Van Buren, & Kahan, 1988). One study indicated that 78% of cases of renal graft failure in the second year after transplant were believed to be due to nonadherence (Kiley, Lam, & Pollak, 1993).

Unlike some other medical regimens, no gold standard has been identified to assess regimen adherence in renal transplant patients. Blood levels of the most common immunosuppressive medications (e.g., cyclosporine) are quite unstable over time and are influenced by a number of factors other than medication adherence (e.g., food intake, other medications). Thus, reliably determining the rate of nonadherence through the use of biochemical markers is difficult in this population (Lemaire, Fahr, & Maurer, 1990). The large majority of past studies involving transplant patients have simply relied on patient self-reports of adherence behavior (e.g., De Geest et al., 1995; Rovelli et al., 1989; Siegel & Greenstein, 1997). Given the difficulties in assessing adherence in this population, it is not surprising that estimates of nonadherence have varied greatly, ranging from less than 5% to as many as 75% of patients (De Geest et al., 1995; Didlake et al., 1988; Greenstein & Siegal, 1998; Kiley et al., 1993; Rovelli et al., 1989; Siegal & Greenstein, 1997; Sketris, Waite, Grobler, West, & Gerus, 1994).

A promising advancement in adherence assessment involves the use of electronic monitoring of medication dosing (Blowey et al., 1997). Utilizing this methodology, Blowey et al. reported that 26% of the pediatric renal transplant recipients studied missed three or more consecutive cyclosporine doses over a 2–3 month assessment period. Of interest, only half of the patients who were classified as noncompliant according to electronic dosing records were similarly classified using other common strategies (i.e., physician or nurse ratings, adherence estimates based on blood levels of cyclosporine). Clearly, all available adherence measures and assessment methodologies used in both transplant and dialysis samples have important limitations. Given these limitations, we believe it is critical for researchers to use multiple indicators of regimen adherence to minimize the impact of the limitations or idiosyncrasies of a single methodology.

Determinants of Adherence

Social support. A range of clinical, sociodemographic, and psychosocial factors have been examined as potential correlates or determinants of ESRD patient adherence behavior. Considerable evidence in other populations suggests that the availability and perceived quality of social resources are important correlates of regimen adherence (e.g., Kulik & Mahler, 1993; B. S. Wallston, Alagna, DeVellis, & DeVellis, 1983). Limited research is available regarding adherence among ESRD patients. Christensen et al. (1992) examined the effects of social support in the family and illness-related stress on hemodialysis patient adherence. Results indicated that patients holding perceptions of a more supportive family environment, characterized by greater cohesion and expressiveness among family members and less intrafamily conflict, exhibited significantly more favorable adherence to fluid-intake restrictions than did patients reporting less family support. In this same study, family support was not associated with adherence to dietary restrictions. Other research has suggested that more favorable marital adjustment among center hemodialysis patients and their spouses is also related to better fluid-intake but not dietary adherence (Somer & Tucker, 1988, 1992).

Several studies involving samples of center hemodialysis patients have found that social support was not related to biochemical markers of fluid-intake or medication adherence among dialysis patients (Boyer, Friend, Chlouverakis, & Kaloyanides, 1990; Cummings, Becker, Kirscht, & Levin, 1982; Hitchcock, Brantley, Jones, & McKnight, 1992). Similarly, a recent study of adherence among renal transplant patients failed to demonstrate a significant effect for patients' social resources (Rudman, Gonzales, & Borgida, 1999). Kimmel et al. (1995) suggested the possibility of gender differences in the association of support with adherence. In a study of 149 center hemodialysis patients, a significant association between greater perceived support and more favorable medication adherence was obtained among males but not females. Results of a study by our group (Moran et al., 1997) suggested that the association between support and adherence might be moderated by individual differences in trait conscientiousness. Clearly, additional research is needed to clarify what seems to be a complex association between social support and patient adherence.

Cognitive factors. In the broader health behavior literature, cognitive factors have long played a central role as possible predictors of health-related behavior (Rosenstock, 1966; K. A. Wallston & Wallston, 1982). However, research examining the influence of cognitive factors on ESRD patient adherence has been markedly inconsistent across both studies and measures. There is evidence to suggest that self-efficacy expectations are related to both fluid-intake and medication adherence among dialysis patients as well as medication adherence among transplanted patients (Brady, Tucker, Alfino, Tarrant, & Finlayson, 1997; Christensen, Wiebe, Benotsch, & Lawton, 1996; De Geest et al., 1995; Eitel, Friend, Griffin, & Wadhwa, 1998; Rosenbaum & Ben-Ari Smira, 1986; Schneider et al., 1991). In a study of 40 hemodialysis patients, Eitel and colleagues (1998) reported that adherence-specific self-efficacy expectancies significantly predicted future fluid-intake adherence assessed 3 months later. However, self-efficacy failed to predict dietary or medication adherence.

Empirically and conceptually related to the notion of self-efficacy expectations is the construct of locus of control. There is modest evidence that patients with an internal locus of control exhibit more favorable regimen adherence (Kaplan De-Nour & Czaczkes, 1972; Poll & Kaplan De-Nour, 1980; Oldenburg, MacDonald, & Perkins, 1988). However, other research has suggested that internal control expectancies are not significantly related to hemodialysis regimen adherence (Brown & Fitzpatrick, 1988; Schneider et al., 1991; Wittenberg et al., 1983).

A number of studies involving renal dialysis patients have examined components of the health belief model (HBM; Rosenstock, 1966) as predictors of adherence. Research involving both center hemodialysis patients (Cummings et al., 1982; Weed-Collins & Hogan, 1989) and renal transplant patients (Kiley et al., 1993) has reported that greater perceived barriers (e.g., being away from home, medication cost) were associated with poorer medication adherence. However, other cognitive factors composing the HBM (e.g., perceived threat, perceived benefits) have rarely been found to be related to adherence among ESRD patients (Hartman

& Becker, 1978; Rosenbaum & Ben-Ari Smira, 1986; Wiebe & Christensen, 1997).

Personality influences on adherence. In their review of the five-factor model of personality, Wiebe and Christensen (1996) suggested that conscientiousness may be the personality trait most relevant to adherence behavior. The conscientiousness factor has been described as reflecting a highly purposeful, self-disciplined style, high in self-control and constraint (Digman, 1990; McCrae & John, 1992). Correspondingly, adherence investigators have characterized nonadherence as a self-control problem, citing low frustration tolerance, inability to delay gratification, and acting out as underlying causes of nonadherence (Kaplan De-Nour & Czaczkes, 1972; Rosenbaum & Ben-Ari Smira, 1986).

Empirical evidence linking the conscientiousness trait to adherence remains limited. In a study of 72 renal dialysis patients, Christensen and Smith (1995) reported that higher conscientiousness scores from the NEO Five-Factor Inventory (Costa & McCrae, 1992) were significantly associated with more favorable medication adherence (i.e., lower serum P values) after controlling for a number of demographic factors. However, in two later studies conducted by our group, conscientiousness failed to exert a direct effect on fluid-intake or medication adherence (Moran et al., 1997; Wiebe & Christensen, 1997).

Another personality factor that may have implications for adherence behavior is trait hostility. Christensen, Wiebe, and Lawton (1997) examined individual differences on the Cook-Medley (1954) hostility (Ho) scale as a potential determinant of dialysis regimen adherence. Christensen et al. argued that the generally suspicious, mistrusting, and cynical style of high scorers on the Ho scale may predispose them to reject or disregard the direction of their renal care providers. Consistent with this notion, Christensen et al. obtained a significant main effect between higher Ho scale scores and poorer adherence to the phosphorus control regimen. Moderational analyses indicated that the deleterious effect of hostility on adherence was most pronounced among patients possessing the expectancy that positive health outcomes are not contingent on the actions or advice of health care providers (i.e., low powerful-others health locus of control). In other words, the generally mistrustful nature of cynically hostile patients seemed to be most deleterious among those individuals who held the specific belief that the actions of their health care providers fail to influence health outcomes in a positive way. Again, however, results failed to generalize across multiple adherence domains. Neither hostility nor patient expectancies were significantly associated with fluid-intake adherence in this study.

Patient × Treatment Interactions and Adherence

Research involving predictors of adherence in this and other chronic disease populations has produced inconsistent findings (Kaplan & Simon, 1990). Our own research team has argued that the association of patient individual differences and adherence can be clarified by considering the interactive association of patient characteristics with features of the illness and medical treatment context (i.e., the Patient × Context interactive framework; Christensen, 2000; Wiebe & Christensen, 1996). From an interactional perspective, adherence should be best when the patient's characteristic or preferred style of coping with illness-related stress is consistent with the contextual features or demands of the particular type of medical intervention the patient is undergoing. For example, in two studies comparing samples of staff-treated center hemodialysis and self-treated home dialysis patients, adherence was maximized in cases in which the patients' preferred styles of coping matched the requirements or demands of the type of dialysis treatment received (Christensen, Smith, Turner, & Cundick, 1994; Christensen, Smith, Turner, Holman, & Gregory, 1990). That is, patients with highly active or vigilant coping styles exhibited better adherence when undergoing renal treatment that is primarily patient controlled and carried out at home (i.e., CAPD or home hemodialysis). Patients with less active or more avoidant styles of dealing with stress exhibited more favorable adherence when undergoing staff-administered treatment in a hospital or clinic (i.e., center hemodialysis).

The vast majority of adherence studies in this population have relied on cross-sectional assessment of patient characteristics and adherence outcomes (see exceptions by Christensen, Smith, et al., 1994; Friend, Hatchett, Schneider, & Wadhwa, 1997; Schneider et al., 1991). A cross-sectional approach obviously limits the extent to which causal inferences can be drawn. A related limitation found in past research involves the fact that patient characteristics are typically assessed after patients reach the "end stage" of renal insufficiency and are receiving some form of renal replacement intervention to treat the disease. Causal interpretations using this type of design are particularly difficult because the assessment of patient characteristics is confounded with the patient's medical condition and treatment history. Unfortunately, chronic illness researchers have few opportunities to assess patients prior to the onset of the illness of interest.

In our own ongoing work involving ESRD patients, we have begun identifying patients at an early, asymptomatic stage in the progression of renal insufficiency and then following patients prospectively until renal replacement intervention is necessary. For the majority of patients with chronic renal failure, ESRD is the end result of a progressive deterioration in kidney function over a period of months or years. Identifying future ESRD patients who are at an early stage of renal insufficiency provides a unique opportunity to prospectively test hypotheses concerning the prediction of adherence to a future regimen.

Our initial work using this methodology examined 69 patients first assessed in the early, asymptomatic stages of renal insufficiency (Christensen, Moran, & Ehlers, 1999). All patients had a form of progressive renal disease and were identified on the basis of routine screening of renal function (i.e., serum creatinine levels > 3.5). Patients' degree of "information vigilance" was assessed using a composite measure consisting of the Information Preference subscale from the Krantz Health Opinion Survey (Krantz, Baum, & Wideman, 1980), the Internal Health Locus of Control Scale from the Multidimensional Health Locus of Control Scales (K. A. Wallston, Wallston, & DeVellis, 1978), and the Monitoring subscale from the Miller Behavioral Style Scale (Miller, 1987). Higher information vigilance scores were defined by higher scores on each of these component measures. Patients were reassessed approximately 24 months after this pre-ESRD assessment. Results indicated that among home dialysis patients, individuals reporting higher information vigilance scores prior to the onset of ESRD displayed better fluid-intake adherence relative to low-information-vigilance patients. Among center hemodialysis patients, an essentially opposite pattern was observed. That is, patients possessing a more information-vigilant style displayed poorer adherence (higher IWG) when undergoing the provider-directed, hospital-based treatment. Thus, consistent with the interactive framework, the degree of congruence between patients' characteristic style of coping and the demands or requirement of the type of dialysis eventually prescribed predicted regimen adherence.

Adherence Intervention Research

Given the prevalence and clinical importance of adherence among ESRD patients, the design and evaluation of interventions to improve adherence is critically important. Most ESRD adherence intervention studies have used behaviorally oriented techniques. There is evidence to suggest that a range of behavioral strategies (e.g., self-monitoring, behavioral contracting, and positive reinforcement) are associated with improved adherence among hemodialysis patients (Barnes, 1976; Brantley, Mosley, Bruce, McKnight, & Jones, 1990; Carton & Schweitzer, 1996; Hart, 1979; Hegel, Ayllon, Thiel, & Oulton, 1992; Keane, Prue, & Collins, 1981). However, most of these studies are limited to single-subject or very small sample designs. A notable exception is a study that evaluated interventions to facilitate adherence among 87 hemodialysis patients (Cummings, Becker, Kirscht, & Levin, 1981). These authors reported that several behavioral techniques, including behavioral contracting and the use of various types of positive reinforcement (i.e., lottery tickets or verbal reinforcement), were associated with significant improvement in both fluid-intake and medication adherence immediately following a 6-week intervention period. However, these improvements did not persist at a 3-month follow-up assessment.

In our own recent work we examined the efficacy of a behaviorally based, self-regulation intervention designed to increase adherence to fluid-intake restrictions among hemodialysis patients (Christensen, Moran, Wiebe, Ehlers, & Lawton, in press). Components of the intervention protocol were largely derived from Kanfer's theory of the self-regulation of behavior (Kanfer & Gaelick, 1986). In this effort, 20 center-hemodialysis patients received the self-management intervention, with each patient being matched to a no-treatment control patient of the same gender, diabetic status, approximate time on dialysis, and approximate age. Patients assigned to the self-management condition participated in 7 weekly hour-long treatment sessions conducted in small groups. The primary focus of the sessions was instructing patients in the self-monitoring, self-evaluation, and self-reinforcement of fluid-intake behavior. Patients in the two groups exhibited a significantly different pattern of change in fluid-intake adherence across the 8-week follow-up period. The intervention and control groups did not differ significantly in terms of adherence at baseline or in the initial 2 weeks following completion of the intervention. However, differences were statistically significant at the 8-week follow-up assessment, with the intervention group displaying better adherence (lower interdialysis weight gains) than the control group. Although the group difference at the 8-week assessment was statistically significant, the mean level of fluid-intake adherence (mean IWG $=$ 2.88 kg) in the intervention group still fell in the clinically problematic range. Although the association between degree of nonadherence to fluid restrictions and the risk of complications is thought to be linear in nature, the fact that the intervention group still displayed generally poor adherence at follow-up might be interpreted as evidence that the clinical significance of the effect was limited (Kendall, Marrs-Garcia, Nath, & Sheldrick, 1999). Although intervention studies involving ESRD patients have generally not explicitly evaluated the clinical significance of an intervention effect, it is important for future intervention research to explicitly incorporate some examination of clinical significance into research designs (Jacobson, Roberts, Berns, & McGlinchey, 1999; Kendall, Marrs-Garcia, Nath, & Sheldrick, 1999).

Further research involving a broader range of intervention techniques is also clearly needed before determinations about the most effective strategies in this population can be made. For example, cognitive intervention has been shown to be effective in addressing a range of behavioral disorders but has not been examined as a possible approach to facilitating medical regimen adherence. Results of one recent study involving diabetic patients indicated that the presence of irrational or distorted health-related beliefs was a significant predictor of patient nonadherence (Christensen, Moran, & Wiebe, 1999). These data suggest that cognitive change programs directed toward the identification and modification of maladaptive, distorted thinking may be an important tool in adherence-behavior change.

Psychological Distress, Depression, and Quality of Life in ESRD

Psychological distress and disorder represent a significant detriment to ESRD patient quality of life. A relatively early study found that levels of depression in ESRD were comparable to those observed in other chronic illnesses (Cassileth et al., 1984). More recent epidemiologic evidence suggests that the rate of psychiatric disorders in the ESRD population is substantially higher than that observed in other chronic medical conditions (Kimmel, Thamer, Richard, & Ray, 1998). In this study of Medicare enrollees, Kimmel and colleagues reported that hospitalization rates for psychiatric disorders were over twice as high for ESRD patients compared with non-ESRD patients with diabetes, ischemic heart disease, or cerebrovascular disease. Mood disorders, dementia, and substance-use disorders were the most common psychiatric illnesses among ESRD patients.

Estimates of the prevalence of depression in this population are particularly high, suggesting that 12–40% of ESRD patients meet diagnostic criteria for a mood disorder (Craven, Rodin, & Johnson, 1987; Craven, Rodin, & Littlefield, 1988, Hinrichsen, Lieberman, Pollack, & Sternberg, 1989; Lowry & Atcherson, 1980). There is some indication that depression symptoms are highest among patients treated with center hemodialysis and somewhat lower among patients with a functioning renal graft (Christensen, Holman, et al., 1991). The substantial variation in depression estimates is likely due to differences in the assessment method and diagnostic criteria used. For example, Craven et al. (1988) reported that 45% of their ESRD sample was identified as depressed using the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961; BDI score greater than 10), but only 12% were diagnosed with a depressive disorder using a clinical interview and criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed., *DSM–III*).

Depression Assessment in ESRD

The assessment and diagnosis of depression in ESRD patients is problematic owing to the confound between somatic symptoms of depression and physical symptoms of renal failure and side effects of ESRD treatment. Neurovegetative symptoms of depression, including fatigability, cognitive deficits, decreased appetite, insomnia, and loss of libido, can occur secondary to chronic renal failure and in the absence of a depressive syndrome. Moreover, conditions associated with ESRD such as anemia, electrolyte disturbances, and underlying systemic disease (e.g., diabetes) may mimic depressive symptoms. In addition, ESRD patients may take medications such as antihypertensives and corticosteroids, which can produce mood-altering effects.

Considerable evidence suggests that nonsomatic or cognitive symptoms of depression more accurately discriminate depressed from nondepressed ESRD patients than do somatic criteria (Craven et al., 1987; Hinrichsen et al., 1989; O'Donnell & Chung, 1997). For example, in a study of depression assessment using *DSM–III–R* criteria, Craven et al. (1987) reported that depressed mood, loss of interest, guilt, and concentration problems were significantly associated with a diagnosis of major depression, whereas only one somatic indicator, appetite and weight changes, showed a specific relationship to major depression among ESRD patients. Other somatic symptoms (e.g., loss of energy, decreased sexual interest) were common in the entire ESRD patient sample and thus were not useful in distinguishing depressed from nondepressed individuals.

Not surprisingly, the prevalence of clinical depression has been shown to vary greatly depending on whether somatic symptoms of mood disorder are included in the diagnostic screening. O'Donnell and Chung (1997) reported that the rate of major depressive disorder among renal dialysis patients dropped from 34% to 6% when somatic indicators were excluded from the *DSM–III–R* assessment criteria. *DSM–IV* criteria dictate that symptoms of depression due to the direct physiological effects of a general medical condition be excluded from consideration when diagnosing a depressive episode (American Psychiatric Association, 1994). This practice has the potential to reduce the "false positive" rate when diagnosing depression in medically ill patients. However, it places great onus on the clinician to judge whether a symptom is a direct consequence of a physical disorder and may result in considerable variance in clinical judgment (O'Donnell & Chung, 1997). The assessment of depression in all medically ill populations is an important and complex issue that clearly deserves more attention from clinical researchers.

Psychosocial Influences on Depression

Patient control appraisals. A diagnosis of ESRD entails a variety of chronic, recurrent stressors, significant change in lifestyle, disruption of familial roles and social identity, and threatened personal control. Much of the research involving determinants of depression has focused on the considerable loss of control encountered by ESRD patients. One of the most salient examples of loss of control occurs when a renal transplant patient experiences organ rejection and subsequent graft failure. Accordingly, there is some evidence that depression is especially common among patients experiencing an unsuccessful transplant (Christensen, Holman, Turner & Slaughter, 1989).

Much of the research involving determinants of depression in the ESRD population has focused on individual differences in patients' perceptions of control (e.g., Christensen, Turner, Smith, Holman, & Gregory, 1991; Devins, Binik, Hollomby, Barre, & Guttman, 1981; Devins et al., 1982, 1984). Although the data have not been entirely consistent, studies have generally indicated that stronger control expectancies or beliefs are associated with less emotional distress. For example, Christensen, Turner, et al. (1991) examined the moderating influence of patient control beliefs on depression in a sample of 96 hemodialysis patients. The belief that one's health is controllable (i.e., higher internal health locus-of-control scores) was associated with less depression among those patients who had not previously experienced a failed renal transplant. However, stronger internal health locus-of-control expectancies were associated with significantly greater depression for patients who had returned to dialysis following an unsuccessful transplant. An analogous pattern was obtained when the locus-of-control measure reflected a belief in health care providers' ability to influence health outcomes (i.e., powerful-others health locus of control). The interactive nature of this pattern is consistent with other work in the chronic disease literature that suggests the adaptiveness of patients' control appraisals may depend on the degree to which such appraisals are congruent with contextual or situational factors (e.g., Andrykowski & Brady, 1994; Helgeson, 1992).

Perceived illness intrusiveness. Devins et al. (1984) suggested that the degree to which an illness interferes with central life domains is an important determinant of depression. Several studies have established that ESRD patients perceiving greater illness-related disruption of lifestyle and social activities report poorer emotional well-being (Devins et al., 1984; Devins, Beanlands, Mandin, & Paul, 1997; Devins, Mandin, et al., 1990; Sacks, Peterson, & Kimmel, 1990). The effect of perceived intrusiveness on depression appears to persist even after controlling for physical disease severity (Sacks et al., 1990).

In one recent study, Devins et al. (1997) examined the moderating effects of patient self-concept and age on the relationship between illness intrusiveness and distress in a sample of 101 ESRD patients. Devins et al. found that the degrees of illness intrusiveness and emotional distress were significantly and positively correlated in patients who perceived themselves as similar to the stereotypical chronic kidney patient. In contrast, among patients construing themselves as dissimilar from the chronic kidney patient, increasing illness intrusiveness was unrelated to distress. Devins et al. suggested that those ESRD patients whose self-definitions are strongly tied to the illness role may perceive or encounter fewer potentially rewarding, nonillness experiences, and in turn experience greater emotional distress.

In another study involving potential moderators of the illness intrusiveness–distress relationship, Eitel, Hatchett, Friend, Griffin, and Wadhwa (1995) examined the effects of perceived illness intrusiveness and clinician ratings of illness severity on depression in samples of staff-treated center hemodialysis patients and CAPD patients self-treated at home. Severely ill CAPD patients were found to be more depressed and perceived greater illness-related disruptions in social relationships relative to hemodialysis patients also high in severity of disease. Eitel et al. suggested that as medical illness becomes more severe, the greater control over treatment delivery required by the home CAPD treatment may become a burden to very ill patients and their families, resulting in greater illness intrusiveness and ultimately more depression. These findings underscore the importance of jointly considering patient appraisals and contextual variables to understand depression in this population.

Social support. As is the case with other clinical populations, various indices of the quantity and perceived quality of social support have been associated with more favorable psychological adjustment among ESRD patients (Christensen, Turner, Slaughter, & Holman, 1989; Kimmel et al., 1995; Shulman, Pacey, Price, & Spinelli, 1987). A supportive family environment has been identified as a particularly important source of social support for chronically ill individuals (Christensen, Turner, et al., 1989; Christensen, Wiebe, Smith, & Turner, 1994). Christensen, Turner, et al. (1989) examined the effects of perceived familial support and degree of illness-related impairment on emotional adjustment in a sample of 57 renal transplant patients. Severely ill patients perceiving a less supportive family environment (i.e., less cohesion and expressiveness and greater conflict) displayed significantly higher levels of depression and anxiety than patients with a more supportive family environment. However, among patients experiencing relatively low illness-related impairment (and presumably less stress), the effect of family support was not significant.

One often-noted limitation of the social support literature is the absence of data regarding how social resources exert an effect on well-being (e.g., Barrera, 1986; Cohen & Wills, 1985). In a sample of 75 patients awaiting renal transplantation, Moran, Christensen, Ehlers, and Bertolatus (1999) examined the possibility that a potentially beneficial effect of a supportive family environment on emotional distress might be mediated by a reduction in illness-related intrusive thoughts. Data indicated that patients who perceived their family environment as being more conducive to the open expression of stressful thoughts and feelings (higher expressiveness) reported significantly fewer symptoms of both depression and anxiety. Moreover, the effect of this type of support on distress was largely accounted for by a reduction in illness-related intrusive ideation.

ESRD Treatment and Patient Quality of Life

In general, the choice of a particular ESRD treatment modality is substantially influenced by nonmedical factors, including patient and provider preferences and judgments about which modality would be associated with the most favorable patient quality of life (Christensen & Moran, 1998; Davison, 1996; Flechner, 1994). For a small minority of ESRD patients, a particular renal treatment modality may not be medically feasible (e.g., vascular access problems limiting the use of hemodialysis or loss of vision limiting the use of self-directed modalities). However, hemodialysis, peritoneal dialysis, and renal transplantation are all medically acceptable treatment alternatives for the large majority of patients.

A functioning renal graft offers the ESRD patient freedom from frequent, time-consuming, and sometimes painful or uncomfortable dialysis treatments. Not surprisingly, quantitative and descriptive reviews of the literature have generally concluded that a successful renal transplant is associated with higher patient quality of life than any form of renal dialysis (Cameron, Whiteside, Katz, & Devins, 2000; Dew et al., 1997). In a recent meta-analytic review of 49 studies, Cameron et al. reported that renal transplantation was associated with lower emotional distress and greater subjective well-being than either center hemodialysis or CAPD. Although fewer studies have compared ESRD modalities in terms of health-related patient quality of life, there is evidence that transplant patients exhibit less functional impairment, more favorable social functioning, and greater ambulation and mobility than patients receiving dialysis (Christensen, Holman, et al., 1989, 1991; Dew et al., 1997; Evans et al., 1985). There is also evidence that successfully transplanted patients are more likely to be employed than are dialysis patients (Christensen, Holman, et al., 1989; Evans et al., 1985). Most studies comparing quality of life across ESRD treatments have attempted to statistically control for clinical or demographic “case mix” differences. Nevertheless, between-modality differences in patient age, education, comorbidity, disease severity, and a variety of other confounding factors make it difficult to draw firm conclusions about the quality-of-life superiority of one ESRD modality over another.

As Dew and colleagues (1997) noted, even when a between-treatment quality-of-life advantage is observed for renal transplantation, significant within-treatment variance typically exists and a number of individual patients in a given sample may show little or no gain in quality of life following successful transplantation. Moreover, because of a perennial shortage of donor organs, renal transplantation remains a scarce medical resource and requires clinicians to make difficult organ allocation decisions. Because of this variability in patient outcomes and the limited supply of donor organs, identifying predictors of transplant-related changes in quality of life is a potentially important part of the clinical management and treatment decision making involving ESRD patients. Despite an absence of empirical data, the clinical literature suggests that psychosocial factors are often considered as part of the multidisciplinary transplant recipient evaluation and selection process (Levy, 1994; Ramos, Kasiske, & Danovitch, 1998). An important part of this evaluation is an attempt to determine which patients are likely to realize significant gains in quality of life following transplantation. Unfortunately, there remains little empirical foundation for practitioners to draw from when making judgments about patient suitability based on psychosocial criteria.

Our research team recently examined the possibility that changes in emotional well-being following renal transplantation would vary as a function of patient coping preferences (Christensen, Ehlers, Raichle, Bertolatus, & Lawton, 2000). Sixty patients were initially assessed using the Krantz Health Opinion Survey and the BDI while on the waiting list for a cadaveric renal transplant. Patients were reassessed approximately 12 months later. Among patients receiving a transplant during the follow-up period, those with a high preference for seeking and receiving health-related information exhibited a substantial reduction in depression following transplantation. In contrast, patients relatively low in preference for information showed a slight increase in depression. This pattern is consistent with research involving renal dialysis patients, suggesting that individuals with more vigilant or active coping styles exhibit more favorable adjustment when undergoing medical interventions that offer a relatively high degree of patient autonomy and control. These findings also suggest that a formal assessment of patients’ health-related coping preferences may assist practitioners in identifying those ESRD patients particularly well suited for the unique challenges and potential benefits associated with renal transplantation.

The Treatment of Depression and Distress in ESRD

Despite the high prevalence of depression among ESRD patients, interventions designed to increase emotional well-being have received little empirical attention. In a novel intervention study, Leake, Friend, and Wadhwa (1999) tested the effects of experimentally manipulated self-presentations on the adjustment of center hemodialysis patients. Patients randomly assigned to selectively present themselves as successful copers during a videotaped interview (ostensibly to be used to orient new dialysis patients) reported significantly reduced depression up to 1 month following the study, whereas depression levels among control group patients were largely unchanged. Leake and colleagues suggested that participation in the strategic self-presentation exercise facilitated patients' problem-solving skills and enhanced patients' self-efficacy to deal with the disease leading to the observed reduction in depression.

There is some evidence that both depression and anxiety among ESRD patients can be successfully treated with more conventional psychological interventions (Hener, Weisenberg, & Har-Even, 1996). Hener et al. compared the efficacy of supportive psychotherapy, cognitive–behavioral therapy, and a no-intervention control group in reducing symptoms of depression among hemodialysis patients. Results indicated that both treatment groups experienced significant reductions in depression and anxiety compared with the control group. There were no significant differences in efficacy between the two active treatment groups.

Pharmacological treatment of depression has also been shown to be effective in this population (Surman, 1987). However, many antidepressant medications have side effects that may not be well tolerated by ESRD patients (see review by Kimmel, Weihs, & Peterson, 1993). The added complexities involved in using pharmacologic depression treatments in seriously ill patients with chronic renal impairment clearly increase the need for more careful evaluation of nonpharmacological alternatives.

Biopsychosocial Influences on Morbidity and Mortality

Given that ESRD is typically the end result of a gradual progression of chronic renal insufficiency, there has been considerable interest in identifying factors that influence disease progression in individuals with this condition (Badalamenti & DuBose, 1991; Rahman & Smith, 1998). Although a variety of biomedical factors have been considered as possible mediators of disease progression, few consistent findings have emerged. Control of the underlying disease process in certain patient subgroups (e.g., glycemic control in diabetic patients, blood pressure control in hypertensive patients) has been linked to slowed progression of renal failure and to reduced patient morbidity and mortality more generally (Rahman & Smith, 1998). In addition, amelioration of the anemia that often accompanies renal insufficiency has been demonstrated to have broadly beneficial effects on patient outcomes, whereas malnutrition has been associated with increased patient morbidity and mortality (Badalamenti & DuBose, 1991; Leavey, Strawderman, & Jones, 1998; Levin, 1999).

An emerging body of evidence suggests that enhanced patient education might play a role in slowing the progression of renal failure and delaying the need to initiate dialysis or transplantation (Devins & Binik, 1996). Binik et al. (1993) reported that a brief, enhanced-education intervention focusing on increasing patient knowledge about the basic pathophysiology of kidney disease, the role of dietary management in renal failure, and the options for renal replacement intervention was associated with a 4.6-month delay in the need to initiate renal dialysis compared with a standard-education control group. Potential mechanisms underlying this effect were not examined. One potential contributor to the effect might have involved increased adherence in the enhanced-education condition. In a related study, increased patient education and vocational counseling prior to the initiation of dialysis was related to higher levels of employment after dialysis was started (Rasgon et al., 1993).

In addition to depression being a clear detriment to patient quality of life, several studies suggest that it may also be related to earlier patient mortality (Burton, Kline, Lindsay, & Heidenheim, 1986; Peterson et al., 1991; Shulman, Price, & Spinelli, 1989). Peterson et al. (1991) reported that a cognitive item subset from the BDI (somatic items were eliminated to avoid a confound with disease severity) significantly predicted ESRD patient mortality over a 2-year period. Other studies have failed to replicate a relationship between depression and survival (Christensen, Wiebe, et al., 1994; Devins, Mann, et al., 1990; Husebye, Westlie, Styrovosky, & Kjellstrand, 1987). For example, Kimmel, Peterson, et al. (1998) reported that BDI scores failed to uniquely predict mortality in a sample of 295 hemodialysis patients followed for 2 years.

In the most recently published study involving ESRD patient depression and survival, Kimmel, Peterson, Weihs, Simmens, et al. (2000) reported that initially assessed depression failed to predict mortality in a sample of 295 hemodialysis patients after controlling for demographic and medical risk factors. However, by obtaining six repeated assessments of depression over an average 39-month follow-up period and treating BDI scores as a time-varying covariate, Kimmel and colleagues demonstrated that changes in depression over time did significantly predict patient survival. This pattern suggests that an acute worsening of mood (or a transitory improvement in mood) may have particularly important implications for patient mortality. Although data concerning the effect of depression on survival are not entirely consistent, we believe the evidence is sufficient to indicate that depression should be considered along with more traditional (biomedical) mortality risk factors.

A very recent study from our group suggests that patient personality may also play a role in influencing patient longevity (Christensen, Ehlers, et al., in press). We examined the potential effect of individual differences in trait neuroticism or chronic negative affectivity and trait conscientiousness on mortality among patients with chronic renal disease. Neuroticism and conscientiousness scores obtained using the NEO Five-Factor Inventory (Costa & McCrae, 1992) uniquely and significantly predicted survival across an average 49-month follow-up period after controlling for the significant effects of age, diabetic status, renal replacement status, and anemia (hemoglobin level). The estimated mortality rate for patients with trait neuroticism scores one standard deviation above the mean was 37.5% higher than for patients with average scores on this dimension. For patients with trait conscientiousness scores one standard deviation below the mean, the estimated mortality rate was 36.4% higher relative to average scorers.

Increasing evidence suggests that the perceived quality of social support or social relationships available to the patient may also be an important predictor of survival. Kimmel, Peterson, et al. (1998) reported that perceived social support was a significant predictor of patient mortality after controlling for patient age, disease severity, and serum albumin level (an indicator of nutritional status). Similar results were obtained by Christensen, Wiebe, et al. (1994) in a study examining the association of perceived family support with hemodialysis patient survival. Among patients classified on the Moos Family Environment Scale (Moos & Moos, 1986) as having a less supportive family environment, estimated 5-year mortality rates were nearly three times higher than estimated mortality for high-support patients. The effect of family support was independent of the significant predictive influence of age and blood urea nitrogen levels. In the most recently published study, Kimmel, Peterson, Weihs, Shidler, et al. (2000) reported a significant association between dyadic relationship quality and ESRD patient survival. Among female patients, higher relationship satisfaction and lower conflict were associated with decreased mortality risk. It is interesting to note that an effect of relationship quality and survival was not obtained for male patients.

The potential effect of psychosocial intervention or applied social support on ESRD patient mortality has not been adequately addressed. Results of a study by Friend, Singletary, Mendell, and Nurse (1986) suggested that participation in a supportive group intervention may prolong survival among hemodialysis patients. Hemodialysis patients participating in a largely unstructured patient support group were significantly more likely to be alive at the end of a 10-year follow-up period compared with nonparticipants. Although this study was uncontrolled (e.g., there was no random assignment or control group comparison), the data underscore the need for further research examining the salutary influence of applied social support.

Adherence Behavior, Treatment Termination, and Patient Mortality

An important unanswered question regarding the effects of depression and social support involves the mediational mechanisms that may account for the influence of these factors on patient mortality. In the general social support and health literature, individual differences in health behavior are often implicated as a potential mediator of the association between support and physical health (Cohen, 1988). Indirect evidence for such an effect in the ESRD population can be found in studies linking social support to adherence behavior (e.g., Christensen et al., 1992) as well as in studies reporting an association between patient nonadherence and earlier mortality (e.g., Kimmel, Peterson, et al., 1998; Kimmel, Varela, et al., 2000; Leggat et al., 1998). However, in a direct examination of the potential mediating role of regimen adherence, we found no evidence that individual differences in adherence account for the association between social support and ESRD patient mortality (Christensen, Wiebe, et al., 1994).

Previous authors have proposed that regimen nonadherence may mediate an effect of depression on mortality (see review by Kimmel et al., 1993). However, research has generally failed to find an association between depression, or negative mood more generally, and patient adherence, suggesting that a mediating role for adherence behavior is unlikely (Christensen, Wiebe, et al., 1994; Friend, Hatchett, Schneider, & Wadhwa, 1997; Simoni, Asarnow, Munford, Koprowski, Belin, & Salusky, 1997). However, one recent study reported evidence that depressed mood in this population may contribute to undernourishment and malnutrition, both of which are important risk factors for premature death in this population (Friend, Hatchett, Wadhwa, & Suh, 1997). Friend and colleagues reported that higher BDI scores were associated with reductions in serum albumin levels (a marker of nutritional status) over time. This finding raises the possibility that although regimen adherence may not account for the association between depression and mortality, other behavioral factors (e.g., nutrional behavior) may play a role.

Although the issue has received scant empirical attention, depression is likely to play a role in influencing patient decisions to terminate dialysis treatment (see Kimmel et al., 1993). Previous data suggest that 11–22% of renal dialysis patient deaths are due to a decision to withdraw from treatment (Neu & Kjellstrand, 1986; Port, Wolfe, Hawthorne, & Ferguson, 1989). Surprisingly, we are aware of no data examining the extent to which symptoms of depression contribute to this process or the extent to which the successful treatment of depression might influence termination decisions. Patient withdrawal from a life-sustaining medical treatment such as renal dialysis is an issue complicated by a number of ethical and legal factors. Nevertheless, given the high likelihood that clinical depression plays a role in influencing patient and provider judgments about treatment termination, this issue clearly warrants additional attention from behavioral medicine clinicians and researchers.

Concluding Observations

Although it is understudied relative to cardiovascular disease, cancer, and other stalwarts of behavioral medicine, ESRD and its treatment reflect a clinically relevant and theoretically intriguing chronic disease context. ESRD is a disorder marked by an extreme loss of personal control, an array of acute and chronic stressors, a high degree of emotional distress and psychiatric comorbidity, and the challenge of lifelong behavioral change. Past research provides an empirical basis for identifying patients at risk for regimen nonadherence or emotional distress, both of which have been linked to increased patient morbidity and earlier mortality. Moreover, a growing body of literature suggests that patient outcomes might be enhanced by using psychological assessment data to inform the renal treatment decision-making process.

Important challenges for future behavioral medicine research and practice include establishing clearer, empirically supported guidelines for the psychological assessment and evaluation of ESRD patients. Differentiating mood disorder from physical sequelae of disease and developing strategies to more accurately evaluate patient regimen adherence are two important goals for future assessment research. Equally important is the need for additional clinical intervention research. Increased attention to the design and evaluation of psychological intervention strategies in this population has the potential to contribute to enhanced patient adherence, improved emotional well-being, and, ultimately, prolonged patient survival.

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