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Integrating Co-Morbid Depression and Chronic Physical Disease Management: Identifying and Resolving Failures in Self-Regulation

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Abstract

Research suggests that treatments for depression among individuals with chronic physical disease do not improve disease outcomes significantly, and chronic disease management programs do not necessarily improve mood. For individuals experiencing co-morbid depression and chronic physical disease, demands on the self-regulation system are compounded, leading to a rapid depletion of self-regulatory resources. Because disease and depression management are not integrated, patients lack the understanding needed to prioritize self-regulatory goals in a way that makes disease and depression management synergistic. A framework in which the management of co-morbidity is considered alongside the management of either condition alone offers benefits to researchers and practitioners and may help improve clinical outcomes.

Depression is common among individuals with chronic physical disease (Anderson, Freedland, Clouse, & Lustman, 2001; Aromaa et al., 1994; Ciesla & Roberts, 2001; Dickens, McGowan, Clark-Carter, & Creed, 2002). Independently, both depression (i.e., major depression or elevated depressive symptoms) and chronic physical diseases such as such as asthma, arthritis, cardiovascular disease, diabetes, and HIV/AIDS significantly interfere with life functioning, including decreased work productivity and loss of social functioning (Hays, Wells, Sherbourne, Rogers, & Spritzer, 1995; Hoffman, Rice, & Sung, 1996; Stewart, Ricci, Chee, Hahn, & Morganstein, 2003; Wells & Sherbourne, 1999). Further, just as chronic physical diseases cannot be “cured,” depression is often a chronic disorder with a high likelihood of relapse (Solomon et al., 2000). When occurring together, depression and chronic physical disease may result in particularly poor clinical outcomes as compared to either condition alone, including

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increased risk for disability, hospitalization, and early mortality (for reviews, see Evans et al., 1999; Krishnan et al., 2002).

In an effort to understand the connection between depression and chronic physical disease, many theorists and researchers have suggested a direct physiological link by which each of these conditions may cause and exacerbate the other. For example, depression is associated with reduced heart rate variability, increased sympathetic nervous system activity, and platelet aggregation, all of which are risk factors for cardiovascular disease (Musselman, Evans, & Nemeroff, 1998); and conversely, cardiovascular disease may be associated with the elevation of pro-inflammatory cytokines (Blum & Miller, 1998) that perpetuate depression (Appels, Bar, Bar, Bruggeman, & De Baets, 2000). Direct causal physiological mechanisms also have been proposed between depression and a range of other chronic diseases (Jacobson, Samson, Weinger, & Ryan, 2002; Krishnan et al., 2002).

Based in part on this proposed causal link, it is logical to assume that improvement of one condition (i.e., depression or chronic physical disease) should improve the other condition through an alteration of physiological mechanisms. Accordingly, there has been mounting interest in the hypotheses that depression treatment programs will improve chronic physical disease outcomes and that chronic disease management will improve depressed mood. In the current paper, we explore whether these hypotheses are supported by the treatment outcome data for individuals with co-morbid[1] chronic disease and depression, sampling from empirically supported treatments of depression, psycho-educational disease management programs, and medication-based disease management programs. The theoretical, methodological, and practical issues associated with the mechanisms that link depression and chronic physical disease are explored, with a focus on the management of these co-occurring conditions (e.g., Carney et al., 1999;Frasure-Smith & Lesperance, 2003a;Frasure-Smith & Lesperance, 2003b;Lustman & Clouse, 2002). In light of the findings presented in the treatment outcome literature, a model for integrating patients' treatment-related cognitive representations, behavioral responses, and social functioning is proposed, with the goal of improving both the major depressive disorder and the symptoms of chronic disease.

The Effects of Depression Management on Disease

Several researchers have suggested that depression causes or exacerbates chronic physical disease. Evidence for the causal link also has been drawn from studies that have identified either major depression or elevated depressive symptoms as a risk factor for the development of chronic diseases such as coronary heart disease (Ruguiles, 2002; Wulsin & Singal, 2003). Further, several studies suggest that depression predicts mortality in samples of patients with myocardial infarction (Bush et al., 2001; Ladwig, Kieser, Konig, Breithardt, & Borggrefe, 1991; Lesperance, Frasure-Smith, Talajic, & Bourassa, 2002; Welin, Lappas, & Wilhelmsen, 2000), coronary artery disease (Barefoot et al., 1996), stroke (Morris, Robinson, Andrzejewski, Samuels, & Price, 1993), congestive heart failure (Jiang et al., 2001; Murberg, Bru, Svebak, Tverteras, & Aarsland, 1999), diabetes (Black & Markides, 1999), cancer (Derogatis, Albeloff, & Melisaratos, 1979), and HIV/AIDS (Cook et al., 2004; Ickovics et al., 2001; Mayne, Vittinghoff, Chesney, Barrett, & Coates, 1996).

Based on the hypothesis that depression causes and exacerbates chronic physical disease, there has been an assumption that modifying depression through anti-depressant medication or psychotherapy should improve chronic disease outcomes. To evaluate this hypothesis, we examined three forms of treatment that have received empirical support for treating depression:

[1]Throughout this paper, when we refer to "co-morbid conditions" or "co-morbidity" we are referring to co-morbid depression and chronic physical disease.

tricyclic anti-depressants (e.g., nortriptyline, imipramine), serotonin reuptake inhibitors (e.g., paroxetine, fluoxetine), and cognitive-behavioral therapy (for reviews, see Thase & Kupfer, 1996; DeRubeis & Crits-Cristoph, 1998). The studies reviewed include several disease categories, including cardiovascular disease, diabetes, HIV/AIDS, and arthritis. All studies were randomized controlled trials that examined the effects of depression treatment not only on depressive symptoms as measured by standardized measures such as the Beck Depression Inventory (BDI; Beck et al., 1979) or Modified Hamilton Rating Scale for Depression (MHRSD, Miller, Bishop, Norman, & Maddever, 1985), but also on "hard" disease outcomes such as mortality or biological indicators of disease progression. These 11 studies are described in Table 1.

Of the 11 studies, several found that the depression treatment significantly improved mood relative to a control; however, there was not a corresponding improvement in chronic physical disease outcome. These findings can be seen in studies of both anti-depressant medication and cognitive-behavioral therapy. For example, Lustman et al. (1997) completed a randomized, placebo controlled, double-blind trial of 68 diabetic patients, 28 of whom had major depression and received either nortriptyline or placebo over 8 weeks of treatment. The reduction in depressive symptoms was significantly greater in depressed patients treated with nortriptyline than with placebo, but patients given nortriptyline were no more likely to have lower glycated hemoglobin levels that patients given placebo. Similarly, Lustman, Freedland, Griffith, and Clouse (2000) conducted a study of sixty patients with either Type I or Type II diabetes and major depression in which individuals were entered into an 8-week trial, randomized to either fluoxetine or placebo. In this trial, reductions in depressive symptoms were significantly better for fluoxetine as measured by both the HRSD and BDI. However, when patients were grouped according to improvement versus lack of improvement in glycemic control, there were no significant differences between fluoxetine and placebo. The Pathways collaborative care study (Katon et al., 2004) found comparable results, with intervention patients (n = 164) reporting improvements in depressive symptoms but not in glycemic control, as compared to usual care patients (n = 165).

Of the large-scale studies in which depression treatment improved mood, there were inconsistent outcomes. For example, the Enhancing Recovery for Coronary Heart Disease (ENRICHD) project was a multi-center, randomized controlled clinical trial that included 1332 depressed patients with coronary heart disease (Berkman et al., 2003). Patients were recruited within 28 days of a heart attack, and diagnosed with either major or minor depression, low social support, or both. Patients were randomized into either a treatment or "usual medical care" group. The "treatment group" received both individual and group CBT for 6 months. Patients in the usual care group received no additional information beyond what they would ordinarily receive from their providers. All patients were referred to a psychiatrist and prescribed anti-depressants as needed. At 6 months, the treatment group had significantly greater reductions in depression, although the effect was small (57% versus 47%). Despite improvements in depression, analyses based on the entire sample of 2,481 patients with either depression or low social support demonstrated that treatment did not result in improved medical outcomes (i.e., lower rates of reinfarction or mortality). After 3 years, 24.4% of patients receiving CBT had died or suffered a second heart attack, as compared to 24.2% of the usual medical care patients. More recent analyses have determined that the intervention had a differential effect on some specific subgroups of the sample, such as white men (Schneiderman et al., 2004), those with refractory depression (Carney et al., 2004), and those taking SSRIs (Taylor et al., 2005). Nonetheless, the overarching conclusion from the ENRICHD study is that treating depression did not consistently improve disease outcomes.

Finally, other studies have found limited efficacy of the depression treatment itself, leading to mixed disease outcome results. For example, the Sertraline Antidepressant Heart Attack

Randomized Trial (SADHART) examined the efficacy of sertraline as compared to placebo among 369 patients with major depressive disorder and a recent myocardial infarction (MI) over the course of 24 weeks (Glassman et al., 2002). Sertraline did not result in improved depression scores as compared to placebo (as measured by scores on the HRSD), although there was significant improvement on a global improvement scale. Further, the use of sertraline did not improve rates of severe cardiovascular events as compared to placebo, although there was a trend suggesting reduced adverse events (cardiac events and mortality), and re-analysis suggests that the treatment group did show improvements in platelet levels (Serebruany et al., 2003). More recently, the Myocardial Infarction and Depression – Intervention Trial (MIND-IT) randomly assigned 331 patients to an intervention group (who were given mirtazapine or citalopram and/or psychotherapy) or a "care as usual" group (van Melle et al., 2007). At 18-month follow-up, there were no statistically significant differences between the antidepressant treatment groups and usual care groups on depressive symptoms (as measured by the BDI and ICD-10) or on cardiac events (including recurrent MI and mortality).

There are several possible explanations for these mostly null and otherwise mixed findings in the literature. Methodological issues may account for some of the findings. For example, issues of power may limit the ability to detect findings across several studies examining depression treatment effects (see Carney & Freedland, 2007). Alternatively, the time frame for assessing medical outcomes may be too brief; that is, 8 weeks is not long enough to observe meaningful changes in either depression or disease. However, the ENRICHD study showed no effect of depression treatment at a 2-year follow-up. Complexities in defining and assessing depression as well as in conducting and interpreting the results of large scale trials also may account for some of the data discussed here (Joynt & O'Connor, 2005). Nonetheless, the overall findings fail to support the notion that there is a physiological or causal link connecting depression treatment to improved chronic physical disease outcomes.

The Effects of Disease Management on Depression

Prior theory and research suggest that the presence of chronic physical disease causes the onset or exacerbation of depressive symptoms and major depression. This hypothesis is supported by studies demonstrating that the presence of chronic physical disease predicts the onset of major depression or an increase in depressive symptoms over time (Aneshensel, Frerichs, & Huba, 1984; Bruce & Hoff, 1994; Cole & Dendukuri, 2003). In addition, several studies demonstrate that the presence of chronic disease predicts poor outcome among individuals with major depression. In one of the largest studies in the field, Moos and colleagues collected an initial sample of 424 depressed individuals from a range of treatment centers. These individuals were assessed at baseline for a range of factors, including Research Diagnostic Criteria for major or minor depression and "medical conditions such as arthritis and asthma" (Billings & Moos, 1985) and were followed over the course of 4 years. The analyses of these data suggested that the presence of medical conditions predicted non-remission of depression at a one-year follow-up (Krantz & Moos, 1988; Billings & Moos, 1985). Further, the presence of medical conditions predicted a "poor course" of depression, a measure including symptom and functioning outcomes, at a 4-year follow-up period (Swindle, Cronkite, & Moos, 1989). Similarly, in an analysis of the Medical Outcomes Study, Sherbourne, Hays, and Wells (1995) examined predictors of the course of depression among 604 initially depressed patients over one year. Individuals with an increased number of chronic medical conditions reported increased depressive symptoms over the one-year follow-up. Additional studies have confirmed these findings (Katon et al., 1994; Murphy, 1983, Tuma, 2000).

Based on the presumption that chronic physical disease causes the onset or exacerbation of depression, one may speculate that improved management of chronic physical disease should result in improved mood. The ideal type of study to examine this issue would be a randomized

controlled trial that involves participants with both depression and chronic physical disease, where both chronic disease and depression outcomes were measured. However, at the time of this writing it appears that no such study has been done. Thus, the current paper reviews randomized controlled trials of the effects of disease management on depression among individuals with chronic disease (who may also have a range of depressive symptoms).

Seven studies of disease management, particularly psycho-education programs (Barlow, Wright, Sheasby, Turner, and Hainsworth, 2002; Weingarten et al., 2002), are included in Table 2. Previous reviews of the literature suggest that psycho-education programs can be efficacious in improving disease management, and thus disease outcomes such as mortality (e.g., Dusseldorp et al., 1999). We define psycho-education as a program providing general education using didactic techniques. Studies that included additional forms of disease management (e.g., behavior therapy, stress management) were not included, as these techniques often are used for depression treatment, and are not a "pure" test of the effects of disease management. Further, two studies of anti-hypertensive medications are highlighted in order to demonstrate the inconsistent effects of medication-based disease management programs. The studies in Table 2 represent randomized controlled trials comparing a disease management program to either a treatment as usual or a placebo control. These studies utilized a standardized measure of depression (e.g., BDI, MHRSD) and cut across a range of chronic physical disease categories (including arthritis, cardiac disease, diabetes, and HIV/AIDS).

The results of this literature are mixed. Several studies of education programs have shown no effect on mood. For example, Lorig, Gonzalez, and Ritter (1999) examined the effect of the Arthritis Self-Management Program (ASMP) on mood among Spanish-speaking patients. A 12-hour educational intervention that consisted of classroom-format discussions of management of arthritis was administered over the course of 6 weeks and compared to a wait-list control. At a 4-month assessment, the patients in the treatment group experienced a significant increase in ratings of self-efficacy to manage their symptoms and in their practice of range of motion exercises. They also experienced a decrease in disability and pain ratings. However, patients in the education program showed no improvement in depression, as measured by the CESD, relative to controls.

Yet some studies do provide evidence that education programs improve levels of depression (Padgett, Mumford, Hynes, & Carter, 1988; Steed, Cooke, & Newman, 2003). For example, a study by Barlow, Turner, and Wright (2000) found that the ASMP program did improve mood in another sample. In this study, 544 people with arthritis were recruited from the community to participate in the ASMP program, delivered for 12 hours over 6 weeks. Three hundred and eleven participants were assigned to the intervention group and 233 were in the control group. At both a 4-month and 12-month follow-up, the ASMP group demonstrated improved depression scores as compared to controls as measured by the Hospital Anxiety and Depression Scale (HADS). Other studies have demonstrated improvements in depressed mood consequent to an education program (see Table 2).

Studies of the effects of medication as compared to placebo on mood have generally reported null findings in reducing depression severity (Beers & Passman, 1990). For example, Rogers et al., (1994) examined the effects of the angiotensin-converting enzyme inhibitor enalapril as compared to placebo on depression among 2,465 patients with symptoms of congestive heart failure enrolled in the Studies of Left Ventricular Dysfunction (SOLVD). Depression was measured by the Profile of Mood States (POMS), and was assessed at baseline, 6 weeks, one-year and two-year follow-ups. Despite evidence that enalapril prolongs life (Riegger, 1993) there were no differences between treatment and control groups on levels of depression. Other studies have found similar results, e.g., Perez-Stable and colleagues (2000) found no differences in depressive symptoms (as measured by the BDI and CESD) at the 12-month

follow-up of a placebo-controlled trial of propranolol among 312 patients with diastolic hypertension.

There certainly could be methodological explanations for the mixed findings. Most importantly, as mentioned earlier, a direct test of the effects of disease management on clinically elevated depressive symptoms has not been undertaken. Thus, it is difficult to determine whether differences across studies in the effects of disease management are related to differences in the efficacy of education programs on disease management. Further, most of these studies did not assess for the presence or duration of anti-depressant treatments, and thus we cannot discern whether patients were receiving care for depression that may influence severity of depressive symptoms. Nonetheless, it is clear from the extant research that an integration of chronic disease and depression management is lacking.

Management of Co-Morbid Conditions as Self-Regulation Failure

So why do treatments for depression generally fail to significantly influence disease outcomes and disease management programs generally fail to significantly improve mood? In 1993, the Agency for Health Care Policy and Research (AHCPR, 1993) published and disseminated practice guidelines for integrating depression screening and treatment into primary care settings. Yet there is a mounting literature suggesting that depression treatment is not integrated into medical care, and it is now well established that despite the availability of therapies, depression remains under-diagnosed (Wells et al., 1989), and under-treated (Steffens et al., 2000; Young, Klap, Sherbourne, & Wells, 2001) in medical settings. The lack of integration may be related to a range of factors, including transportability of diagnostic tools and treatments into medical settings and the additional cost of treating depression (Henk, Katzelnick, Kobak, Griest, & Jefferson, 1996; Wells & Sturm, 1996). Although practice guidelines for general medical disorders are numerous, a recent review of 155 guidelines published by the Agency for Healthcare Research and Quality (AHRQ, 2006; www.ahrq.gov) found that 46% failed to include specific recommendations for depression screening or treatment (Kilbourne, Daugherty, & Pincus, 2007). Of the 83 guidelines that addressed depression, the most common recommendation was for depression screening (advocated by 47% of the 83 guidelines). Strikingly, less than 4% of the 83 guidelines addressed any modifications of medical interventions that should be considered when treating a physical health condition in the context of diagnosed depression (Kilbourne, Daugherty, & Pincus, 2007). Indeed, even when contact is made between different members of a treatment team (e.g., psychiatrist and primary care provider), joint treatment planning is rare (Valenstein et al., 1999), recommendations may not be followed (Shah, Odutoye & De, 2001), and the association among chronic illness, depression, and their respective treatments may not be discussed and understood by patient and families.

Inconsistent findings in the treatment outcome literature reflect a lack of integration of disease and depression management. Currently, depression and chronic physical disease are treated as two, distinct conditions that “ought” to interact. However, researchers and practitioners have not yet linked systematically the pathways between depression and specific chronic diseases, leading to less than optimal management of patients’ co-morbid conditions. Efforts to make the management of co-occurring chronic disease and depression more coordinated and efficient should improve self-regulation (e.g., Leventhal, Meyer, & Nerenz, 1980) and treatment outcome.

Self-regulation is a process whereby individuals create a cognitive representation of the health condition, choose a coping response, and then evaluate the outcome (Leventhal, Meyer, & Nerenz, 1980). Self-regulation in response to a health threat is often difficult, but individuals coping with co-morbidity face some unique challenges that may increase the likelihood that

their self-regulatory efforts will break down. The ways in which depression and its management may concurrently improve and hinder chronic disease outcomes and the ways in which chronic disease and its management may concurrently improve and hinder depression outcomes may be understood in terms of self-regulatory failure. As attempts are made to regulate one's behavior, the total pool of self-control resources gradually may be depleted (Baumeister & Heatherton, 1996). Moreover, a decline in the pool of resources with the onset of a chronic illness leads to the adoption of self-management strategies such as selective optimization for efficient use of reduced resources, particularly in the later years of life (Baltes & Baltes, 1990). Selective optimization is seen in studies of behavioral health that find differences in the rate of seeking health care by elderly versus middle aged adults; in comparison to middle aged adults, adults over 65 years of age avoid worry-related depletion of resources by swiftly seeking medical care and reassurance from practitioners in response to symptoms perceived as potentially threatening (Cameron, Leventhal, & Leventhal, 1993; E.Leventhal, Easterling, Leventhal & Cameron, 1995). The desire to conserve resources expressed by elderly individuals also has been observed to slow down the process of seeking replacements for activities they had given up due to severe health events (Duke, Brownlee, Leventhal & Leventhal, 2002). The data suggest, therefore, that the demands of managing multiple, chronic disorders may prove excessive and debilitating, especially for elderly individuals.

Adding the management demands of a psychological diagnosis for individuals with a chronic physical condition, and/or adding the demands of managing a chronic physical condition for someone managing a psychological disorder, may create excessive demands on the resources for self-management. Difficulties in management and increased emotional distress may arise because of conflict between the procedures for managing a psychological condition and the perception of "safe" management for a physical condition, e.g., a prescription of increased activity conflicts with a drive to conserve resources and avoid symptoms of fatigue due to fear of a cardiovascular event (Eifert, Hodson, Tracey, Seville & Gunawardane, 1996). Specifically, the challenges associated with managing co-morbidity can be described in terms of the *underregulation* and *misregulation* (e.g., Baumeister & Heatherton, 1996; Carver & Scheier, 1981) of illness responses. For individuals with co-morbid conditions, underregulation may occur when there are characteristics of depression that hamper the regulation of chronic disease and/or there are characteristics of chronic disease that hamper the regulation of depression. Self-regulatory failure also can occur because of misregulation, when the successful management of one condition conflicts with the successful management of the other.

Underregulation of Disease Management as a Result of Depressed Mood

The symptoms of depression, such as low energy, poor concentration and poor sleep, may directly interfere with an individual's ability to engage in activities that are central to disease management, resulting in underregulation. Taking the example of a woman with co-morbid depression and diabetes, depression-related deficits in optimism may make her feel as if disease management activities are not worthwhile. Similarly, low energy (characteristic of depression) would make it difficult for her to engage in health behaviors such as regular exercise, monitoring of insulin levels and doctor visits, which are critical to diabetes management. Finally, withdrawal from social support networks would make it difficult for her to receive diabetes-related practical or instrumental support (see Figure 1a).

Depressed individuals experience a range of maladaptive cognitions that may lead to underregulation. Among individuals with chronic physical diseases, depression is associated with lower self-efficacy and lower optimism (Haaga, Dyck, & Ernst, 1991), and each of these may influence behavioral management of chronic disease. For example, both cross-sectional and longitudinal studies have found that low self-efficacy regarding specific disease management behaviors predicts an individual's adherence to behavioral regimens. Cross-

sectional studies suggest that higher self-efficacy regarding diet and exercise is associated with improved adherence to treatment regimens among individuals with chronic diseases such as diabetes (Johnston-Brooks, Lewis, & Garg, 2002; Senecal, Nouwen, & White, 2000). Longitudinal studies also demonstrate that higher self-efficacy predicts improved adherence to behavioral programs. In a study of 110 Type I diabetics, Johnston-Brooks, Lewis, and Garg (2002) found that baseline self-efficacy predicted lower blood glucose levels, and these effects were mediated by the effect of self-efficacy on health behaviors such as diet and exercise. Similarly, Kavanaugh, Gooloey and Wilson (1993) examined the relation among self-efficacy, adherence to diabetic treatment, and glucose levels for 63 diabetic patients over two months. Results showed that increased self-efficacy in the areas of diet, exercise, and glucose testing was a significant predictor of later adherence to diabetes treatment, and that adherence was associated with improved glucose control.

Second, depression may perpetuate lower levels of disease-specific optimism that may result in underregulation through poor adherence to disease management recommendations. For example, Leedham, Meyerowitz, Muirhead and Frist (1995) examined the relation between positive outcome expectations for cardiac transplant patients and adherence to medical regimens (e.g., daily health monitoring, exercise, dietary change) 6 months following transplantation. They found that higher pre-operative expectations predicted improved adherence. Other studies have found that AIDS-specific optimism predicts improved health behaviors among individuals with HIV (Taylor et al., 1992). In a sample of 152 patients prospectively studied for 6 months, Cooper, Lloyd, Weinman, and Jackson (1999) found that non-attendees of cardiac rehabilitation were more likely to believe that they could not control their condition. Overall, these findings suggest that depression may undermine chronic disease management by perpetuating negative cognitions.

Further, several studies suggest that increased depressive symptoms produce fatigue and interfere with activities of daily living (e.g., Stuck et al., 1999). Bruce, Seeman, Merrill, and Blazer (1994) examined a community-based cohort of adults aged 70–79 assessed twice at a 2.5 year interval. Results suggested that high levels of depressive symptoms, as measured by the Hopkins Symptom Checklist at baseline, predicted reduced levels of activities of daily living, adjusting for baseline SES, physical health status, and cognitive functioning. Similarly, in a study of 2,091 male and 3,438 female university students across 16 countries, Allgoewer, Wardle, and Steptoe (2001) found that higher levels of depressive symptoms as measured by the BDI were associated with disruption of activities of daily living, including lack of physical activity and not eating breakfast. These findings imply that symptoms of depression may interfere with activities of daily living, resulting in the underregulation of chronic disease.

Finally, individuals with depression may strain and erode vital social support (Coyne, 1976; Keitner & Miller, 1990), which may be necessary for successful self-regulation. Research has suggested that families of depressed patients report severe levels of dysfunction during the depressive episode (Keitner, Miller, Epstein, Bishop, & Fruzzetti, 1987; Miller, Kabacoff, Keitner, Epstein, & Bishop, 1986). This erosion of family functioning and broader social support may interfere with an individual's ability to engage in behavioral coping with chronic disease. DiMatteo (2004) conducted a meta-analytic review of 122 studies that examined the relation between social support and adherence to medical regimens. Adherence was 1.74 times higher for patients from cohesive families, and 1.53 times lower among patients with high-conflict families. This study further suggested that practical or instrumental support would be particularly helpful in improving disease management. For example, in the case of individuals struggling with heart failure, a family member could remind the individual to take anti-hypertensive medication, prepare low-salt meals, and provide comfort. This suggests that depression's role in undermining social support among individuals with chronic disease also may contribute to underregulation.

Underregulation of Mood Management as a Result of Chronic Disease

Likewise, the onset or exacerbation of chronic physical disease may contribute to the underregulation of depressive symptoms. First, the presence of a chronic and potentially life-threatening illness is likely to perpetuate negative cognitions that are associated with depression. A patient with diabetes may find that symptoms such as painful neuropathy interfere with enjoyable activities and overall life functioning. She also may rely on her support network to help with self-care behaviors, and she may transfer tasks such as buying insulin, driving to appointments, and selecting healthy foods to her spouse or children. Over time, these demands may lead her family to feel burdened and to the erosion of support (see Figure 1b).

The presence of a chronic physical disease, particularly one that is considered life-threatening, perpetuates negative cognitive processes that may increase depression directly (e.g., Beck, Rush, Shaw, & Emery, 1979) and indirectly. Indeed, depression can be caused by and be a symptom of chronic disease. For example, Leung and Bryant (2000) examined patterns of autobiographical memory among 15 patients with insulin-dependent diabetes mellitus as compared to 15 control participants. Based on the Autobiograhical Memory Test, diabetic patients demonstrated impaired access to specific positive memories as compared to controls. In addition, the presence of chronic disease is associated with poorer self-esteem. Bailis and Chipperfield (2002) examined the relation between collective self-esteem (i.e., an evaluation of one's social identity) as well as health locus of control and the presence of chronic physical disease in a sample of 1,267 older adults. Patients with the highest number of chronic conditions were marked by the presence of both lower collective self-esteem and a more external locus of control, suggesting the presence of depressogenic cognitions among individuals with more chronic physical diseases.

In addition, there is mounting evidence suggesting that the symptoms associated with chronic physical disease, such as pain, interfere with behavioral functioning and result in depressed mood (Williamson, 1998). Talbot et al. (1999) conducted a cross-sectional study of 237 adults with type 2 diabetes. In this study, the authors conducted a path analysis suggesting that diabetic complications (e.g., retinopathy) were significantly associated with diabetes intrusiveness (i.e., the extent to which diabetes interfered with life functioning), and diabetes intrusiveness predicted depressive symptoms. Further, in a cross-sectional study of 494 patients with diabetic peripheral neuropathy, Vileikyte and colleagues (2005) assessed the association between the objective indicators of neuropathy severity and depressive symptoms. Neuropathic symptoms of unsteadiness, pain and reduced feeling in the feet mediated this association and accounted for most of the explained variance in depression scores. The association between neuropathic symptoms and depression was in part mediated by related restrictions in activities of daily living and changes in social self perception. Similar findings have been demonstrated among individuals with rheumatoid arthritis (Devins et al., 1993; Neugebauer, Katz, & Pasch, 2003) and cancer (Williamson & Schulz, 1995). These results suggest that symptoms of chronic disease may exacerbate and contribute to the subsequent underregulation of depressed mood.

Finally, chronic physical disease also may burden the individual's support system, undermining the social support required for depression management. There is evidence that families of individuals with chronic physical disease experience significant burden and distress. Over time, these demands may lead to the erosion of support, which in turn may disrupt the patient's activities of daily living (see Lima & Allen, 2001; Oxman & Hull, 1997; Seeman, Bruce, & McAvay, 1996) and make mood management impossible. Evidence from the expressed emotion literature suggests that relatives who experience an increased burden of care are more likely to harbor critical or hostile attitudes towards the patient (Scazufca & Kuipers, 1996). These critical or hostile attitudes among family members predict relapse, especially among depressed patients (Butzlaff & Hooley, 1998). In two prospective studies of spousal caregivers for individuals with chronic disease, Nieboer et al. (1998) found that increased caregiver burden

was associated with increased depression in patients. This basic finding has been replicated in cross-sectional studies (e.g., Lewis, Woods, Hough, & Bensley, 1989), again supporting the contention that characteristics of chronic disease may contribute to the underregulation of depressed mood.

Misregulation of Disease Management as a Result of Mood Repair

Misregulation can be caused by making mistaken assumptions about successful self-regulation, setting unrealistic self-regulatory goals, acting on unimportant or irrelevant parts of the problem (Baumeister & Heatherton, 1996, pp. 9–10), or by misinterpreting physical symptoms and functions. For example, over the past decades, theoretical models of self-regulation of emotion and chronic illness have assumed that patients evaluate the meaning of symptoms and functional changes by comparing these events to underlying prototypes (Leventhal, 1983; Leventhal & Scherer, 1987). The comparison process has been described as involving "if-then" rules (Brownlee, Leventhal, & Leventhal, 2000) or prototype checks (PCs) that compare somatic and functional changes to underlying prototypes (Leventhal, Leventhal & Cameron, 2001). For example, the location, pattern and duration of a symptom are checked against the prototype for everyday acute conditions, such as stress (Bauman, et al, 1989; Cameron, Leventhal & Leventhal, 1995) or a common, acute condition (stomach upset; head cold). If the experienced events do not match these prototypes, they are evaluated against prototypes for a more threatening, and possibly, chronic condition. For example, heart attacks have an expected pattern of severe, sharp pain in chest or arm (pattern and location) that is sudden in onset rather than stable and chronic (time-line). These specific PCs are the units active in matching experience to prototypes (Leventhal, Forster & Leventhal, 2007). As the individual matches symptoms to prototypes of illness based on everyday experience, including prior illness history and observations of illness in others and in the media, the prototypes and matches are frequently inaccurate.

For example, the mismatch to the heart prototype leads to a breakdown in self-management of the symptoms and functional changes of congestive heart failure (i.e., problems breathing while lying down, swollen legs and chronic fatigue mismatch with the expected experiences of chest pain with rapid onset; Horowitz, Rein & Leventhal, 2004). These and other reasons for misregulation may underlie failures in managing co-morbidity. As affective experiences serve as PCs (e.g., feeling good means one is healthy, lacking energy means one is fatigued, aching means one is sick) a depressed patient with co-morbid diabetes may find that as her mood improves, she begins to think that her disease is not so bad after all and that it is more of an acute, rather than chronic, problem. Depression treatment also may lead to behavioral changes such as increased appetite and the subsequent consumption of less healthy foods. Additionally, a patient may try to improve her mood by joining former co-workers for happy hour on Friday nights. Although social interactions may help alleviate depressed mood, exposure to alcohol and unhealthy food choices may directly undermine diabetes management (see Figure 1c).

If depression management is applied successfully, it may interfere with some of the processes that otherwise would have resulted in accurate perceptions of chronic disease symptoms. For example, Ryan et al. (2002) found that diabetic patients with low negative affect had worse detection of hypoglycemic symptoms and less accurate estimates of blood glucose values, as compared to those with high negative affect. Further, Keller, Lipkus, and Rimer (2002) examined the role of depressive symptomatology in perceived risk of getting breast cancer. In this study, participants rated their risk of getting breast cancer before and after receiving either personalized or standard medical risk feedback. Although there were no significant differences in risk estimates at baseline, at follow-up non-depressed individuals did not revise their risks estimates, whereas depressed individuals increased their risk estimates such that they were closer to the estimates provided by the medical feedback.

Individuals who are successful in managing their depression not only may be less likely to perceive the seriousness of the symptoms of chronic disease, but also they may be less likely to perceive the physical disease as chronic and in need of ongoing behavioral management. Non-depressed individuals tend to be less pessimistic and to perceive negative events as less chronic (e.g., Abramson et al., 1978). Individuals who believe that hypertension is an acute or cyclical condition are more likely to minimize the seriousness of high blood pressure, as compared to individuals with a chronic view of hypertension (Croyle, 1990). Indeed, increasing optimism among depressed individuals may inadvertently undermine disease management (Tennen & Affleck, 1987). Holmes and Pace (2002) found that optimistic HIV patients were less likely to be adherent to medication regimens than pessimistic patients, in part because optimists view negative events as transient or acute rather than permanent or chronic (Abramson et al., 1978).

Patients who perceive their chronic disease as acute or cyclical rather than chronic also are likely to doubt the necessity of using preventive behaviors (Horne & Weinman, 2002). Horne and Weinman (1999) examined the relation of illness cognitions to use of preventer inhalers (i.e., use of inhalers regularly, in the absence of symptoms) among 100 community-based asthma patients. Patients who felt that asthma was less chronic perceived less of a necessity for medication. It was shown that perceived treatment necessity mediated the relationship between perceived chronicity and reported adherence. Adams, Pill and Jones (1997) found similar results. Further, this effect appears to maintain over time. Halm, Mora, and Leventhal (2006) interviewed and followed (over a period of six months) 198 adults who had been hospitalized for asthma. The patients were asked whether they thought they had asthma “all of the time” (a chronic view, endorsed by 40% of patients) or “only when having symptoms” (an acute view, endorsed by 53% of patients). The data suggest that an acute view of asthma is associated with unrealistic beliefs about asthma and poor adherence to preventer inhalers across all three time periods (baseline, 1 month, 6 months). Similarly, in a study of 230 patients interviewed about their hypertension, Meyer, Leventhal and Guttmann (1985) carried out a 6-month follow-up interview with newly treated patients. Patients new to treatment were more likely to drop out of treatment if they perceived their condition to be acute. These findings imply that as individuals manage their depression, which includes changing their view that negative events are chronic (e.g., Beck et al., 1979), they may be less likely to engage in healthy behavioral management of chronic disease. In short, treatments for depression may result in the misregulation of chronic disease goals.

Another reason why misregulation of disease management can come about as a result of depression treatment is that the individual may over-prioritize affect regulation (Baumeister & Heatherton, 1996). For example Baumeister and colleagues (e.g., Baumeister, Bratslavsky, Muraven, & Tice, 1998; Muraven, Tice, & Baumeister, 1998) demonstrate in laboratory settings that attempts to regulate affect, including the management of negative moods, can interfere with competing self-regulatory goals, including the performance of physical tasks. Although the emotional and physical challenges experienced in the laboratory may bear little resemblance to health behaviors in the real world, similar hypotheses have been supported in research investigating care seeking among acute coronary syndrome (ACS) and post-MI patients. Specifically, Wong and colleagues (2008) found that ACS patients who reported depression (as measured by the BDI) in their recollection of the 2-week period prior to seeking care were significantly delayed in their presentation for heart attack symptoms. In addition, Bunde and Martin (2006) found that individuals who were coping with depression and its associated fatigue demonstrated slower care seeking following an MI, independent of their cognitive appraisals of the meaning of the MI episode.

The notion that efforts to reduce depression may interfere with disease outcomes also is consistent with the perspective that the emotional system evolved as a mechanism for

promoting survival (Cameron, 2003). The behavioral sequelae of depression may serve as a functional system that reduces energy expenditure and prevents harm (e.g., increased sleep, limited activity; Maier & Watkins, 1998; Nesse, 2000). Individuals with high levels of negative affect (i.e., depression and anxiety) may be more likely to amplify existing symptoms of chronic physical disease (Cohen et al., 1995), enhancing detection of existing symptoms and increasing the likelihood that acute and chronic disease management is carried out. Depressed individuals tend to be self-focused (Ingram, 1990), such that attention may be directed toward mood congruent ruminations, experiences of the body, or both. When sad moods produce body-oriented, self-focused attention, symptoms should be more quickly noticed (Safer, Tharps, Jackson, & Leventhal, 1979). Induced negative mood increases reports of symptoms in physically ill participants (Salovey & Birnbaum, 1989) and healthy participants (Croyle & Uretsky, 1987), whereas happier individuals are less likely to notice these somatic cues (Stretton & Salovey, 1998). Similarly, individuals with high trait negative affectivity may be more likely to detect bodily sensations (Mora et al., 2002; Stegen et al., 2001). This increased vigilance may create a more accurate view of both the presence and seriousness of symptoms ultimately resulting in higher levels of disease management behavior (Kohlmann, 2001).

Finally, depression treatment programs may encourage increased contact with social networks that may undermine disease management. There is now considerable evidence that social relationships may be a source of support, but social relationships also may undermine the individual's self-regulatory efforts (Coyne & DeLongis, 1986). While depression treatment programs may enhance family cohesion and instrumental support, the same support system may inadvertently undermine disease management. For example, several studies have found that individuals in strong social networks are more likely to delay seeking medical intervention (Berkanovic et al., 1981), at least in part due to distrust of the health care delivery system (Suls & Goodkin, 1994). Social networks also may encourage behaviors inconsistent with disease management, e.g., families may expect involvement in holiday feasts, which is inconsistent with the management of chronic illnesses such as diabetes and heart disease. Increases in social contact often associated with depression management may inadvertently increase the maladaptive influences of a support network that discourages help seeking and/or encourages behaviors that undermine disease management.

Misregulation of Mood Repair as a Result of Disease Management

Efforts to manage chronic disease similarly may lead to the misregulation of self-control goals related to depression. A patient with co-morbid depression and diabetes may find that to effectively manage her disease, she must take blood samples throughout the day and avoid appealing foods, leading her to have negative expectations about her self and her future. This patient may report that disease management interferes with life functioning and is depressogenic. Further, she may find that she gets contradictory information from her various health care providers about the importance of her subjective symptoms (i.e., mood) versus her objective symptoms, such as levels of blood hemoglobin (see Figure 1d).

Successful disease management requires an increased awareness of the presence of disease, which may directly perpetuate negative mood, and take focus away from otherwise enjoyable life activities. This is consistent with work by Suls and Fletcher (1985), who suggest that at least in the short-term, more avoidant strategies actually are associated with positive mood. For example, Millar and Millar (1995) conducted a laboratory study in which undergraduate and community-based individuals were asked to think about either a disease detection (e.g., blood pressure checks) or health promoting (e.g., wearing sunscreen) behavior. Individuals asked to think about disease detection reported more negative mood. Previous studies show similar results (Millar & Millar, 1993), and Cioffi (1994) suggests that even disease-focused news of wellness may be associated with negative mood. Additional research suggests knowing

disease status for a greater duration of time (e.g., HIV; Kelly et al., 1993) tends to be associated with increased depression. Disease management programs that increase awareness of the presence of disease, its chronicity, and its consequences may worsen depressed mood and interfere with the successful regulation of depressive symptoms.

Second, disease management behaviors are often difficult and time-consuming (e.g., Safford et al., 2005), and while these behaviors may manage disease, they also distract one from other more desirable life functions. For example, diabetic patients report that they dislike blood monitoring because it can take time from work and leisure activities (Rubin & Peyrot, 2001). Research supports this clinical impression. In a study of the relationship between depression and coronary heart disease in participants with Type I diabetes mellitus, Kinder, Karmack, Baum, and Orchard (2002) examined the cross-sectional relation between insulin measurement and depression. Patients who measured their insulin properly had higher levels of depressive symptoms. In another study of 2,855 subjects, the relation between frequency of blood glucose monitoring and depression was examined. Individuals who never monitored blood glucose had significantly lower depressive symptoms than individuals who tested more than once a day (Franciosi et al, 2001). Further, this effect may be due in part to a disruption in life functioning on the part of the patient. Eitel and colleagues (1995) found in a sample of 98 end-stage renal disease patients that those who were self-administering treatment reported increased depression, and this effect was mediated in part by the extent to which the illness disrupted social functioning. Chronic disease management programs are time consuming and disruptive of life functioning, which may generate a sense of unending entrapment in activities disrupting pursuit of desirable life goals.

Contact with health care professionals may contribute to the misregulation of mood. Patients often report receiving contradictory information from different health professionals, resulting in perceptions of wasted time that could otherwise be used for enjoyable life activities, and a perceived lack of understanding on the part of the providers as to the difficulties of managing a chronic disease (Clark & Gong, 2000; Rubin & Peyrot, 2001). For example, while the American Diabetic Association standard of care is to use physician-coordinated teams, including mental health professionals, more than 90% of patients with diabetes receive care from a primary care physician who does not typically use a team approach (Fore, 1996).

Additionally, there is evidence of discrepancies between patients and providers in their perceptions of the disease. Whereas doctors are more likely to focus on the pathophysiology of a given problem (Cohen et al., 1995), patients may emphasize social implications of their disease. Focusing on the specifics of medical disease management and failing to address how the chronic disease impacts interpersonal relationships may keep patients in a pattern of illness management and denial of the joys of living. Effective communication between practitioners and patients can enhance the efficiency of disease management and the development of strategies for engagement in enjoyable patterns of living that will improve both disease outcome and emotional health (Stewart, 1995). Unfortunately, there is no single, agreed-upon method to optimize doctor-patient interactions (Griffin, Kinmonth, Veltman, Gillard, Grant, & Stewart, 2004). When physicians are trained to handle patients' emotions, patients report significant reductions in emotional distress (Roter, Hall, Kern, Barker, Cole, & Roca, 1995). Such training is not wide-spread, however, and therefore patients may receive incoherent treatment and lack the support they need.

Integrating Depression and Chronic Disease Management

The present research illuminates the central dilemma faced by patients managing co-morbidity: utilizing two separate, self-regulatory goals (i.e., manage disease, manage depression) is problematic. Often, the management of chronic disease and depression overlap or conflict at

the level of lower-order actions or behaviors. Patients rely on subjective cues (e.g., mood, energy level, pain) rather than objective indicators of well-being (e.g., blood pressure). Focusing on subjective cues can backfire when actions aimed at improving these cues are inconsistent with actions that improve objective indicators. For example, if a patient with diabetes and depression experiences a loss of energy (a valid, subjective cue for depression but likely an invalid cue for diabetes) she may identify the symptom as being linked either to the goal of managing depression or of managing diabetes, and that link has implications for the behavioral sequences she chooses (e.g., challenge negative cognitions, raise sugar levels).

The way to integrate disease and depression management best is to create an additional, pragmatic program: to manage co-morbidity. Specifically, researchers and practitioners should strive to identify a set of specifiable conditions under which the treatment for depression will produce effects that are beneficial to the management of chronic physical disease and vice versa. That is, individuals with co-morbidity have three, rather than two, self-regulatory goals. They must attempt to manage their depressed mood, their physical disease, *and* the areas of overlap between these conditions (see Figure 2), while maintaining a view of their co-morbid conditions as chronic, but controllable.

Simply identifying that certain actions are effective in managing both chronic disease and depression is not sufficient. Enhancing a view of the self as active and engaged in goal pursuits related to the ongoing management of co-morbid conditions also is crucial. As Marsh and Craven (2006) describe in their review of the literature on self-concept and performance, "Enhancing skills is not enough; people need to hold positive self-concepts of their abilities in specific areas. …In a wide variety of settings, practitioners who wish to maximize performance are well advised to enhance simultaneously self-concepts and skills in logically related domains (p. 158)." For example, a patient managing co-morbid depression and diabetes must recognize the reasons *why* she is pursuing the goal of managing her co-morbidity, which may include the fact that she wants to have the energy to keep up with her grandchildren, take care of her house, and volunteer for the community throughout the years to come. Achieving the goal of bi-directional improvement in mood and chronic disease will require caregivers to help patients create frameworks that facilitate adaptive disease management behaviors, and this requires overt links among members of the patient's support network (e.g., doctor, psychologist, family).

We are not alone in advocating for a more integrated, comprehensive approach to care for chronic illnesses. For example, Wagner et al. (1996) have developed a heuristic model that addresses the need for patient-centered, evidence-based, collaborative care. This approach focuses on redesigning practice settings, emphasizing patient self-management, increasing access to experts, and providing helpful information about care planning. Wagner and colleagues' approach has influenced the design of programs such as Improving Mood-Promoting Access to Collaborative Treatment (IMPACT; Unützer et al., 2002), a collaborative care management program targeted at people with late-life depression. IMPACT successfully incorporates a multi-dimensional treatment team into depression management in a primary care setting. A randomized controlled trial following 1801 patients over the course of 12 months (Hunkeler et al., 2006) found that IMPACT improves not only mood symptoms, but also indices of physical health, including overall functional impairment and general health ratings (cf. Katon et al., 2004).

Further, we are not alone in promoting the important connections between mood and chronic disease management. Williams and Williams' (1997) created the LifeSkills program, which emphasizes the importance of enhancing communication, strengthening social relationships, and reducing stress as a means to improve health and well-being, especially among individuals at risk for stress-related diseases such as CHD. A recent study (Bishop et al., 2005) found that,

as compared to an information-only control group, patients undergoing coronary artery bypass grafting who participated in LifeSkills not only experienced a significant reduction in depressive symptoms, but also demonstrated significant reductions from baseline to 3-month follow-up in resting heart rate, systolic blood pressure reactivity, and heart rate reactivity.

Despite advances modeled by programs such as IMPACT and LifeSkills, most chronic disease management programs rely on more traditional approaches to care (Wagner et al., 2002), and the field has failed to move from research to widespread implementation of an integrated chronic care model (McEvoy & Barnes, 2007). Additionally, clinically-focused approaches to treating depression among individuals with chronic physical disease fail to focus explicitly on the integration of depression and chronic physical disease management (Franco-Bronson, 1996; Lesperance & Frasure-Smith, 2000; Musselman et al., 1998; Whooley & Simon, 2000). In studies such as those reviewed in the current paper, there was no discussion of how patients perceived the relation between their chronic physical conditions and the negative mood, anhedonia and/or lack of energy that are symptomatic of depression: does the patient see these as separate conditions, as one causing the other, or does s/he see the depressive symptoms as symptoms of the physical condition? Similarly, there was no discussion of whether or how the patient's physicians were involved in depression treatment: did the physician describe the goals of treatment, attempt to integrate the models of depression with the models of chronic illness and/or integrate the two types of treatment regimens? Finally, were goals related to depression treatment designed to be relevant to disease management and vice versa? As a result of poor integration, standard treatments that provide an intervention for depression (i.e., cognitive behavioral therapy, anti-depressant medication) or chronic physical disease (i.e., standard disease management) appear to create treatment regimens for separate and distinct conditions, creating two separate goals for the patient: one for the management of depression and one for the management of chronic physical disease.

In future investigations involving treatment of disease and depression, the particular approach to managing co-morbidity must be made far more explicit. The social systems at work in shaping self-regulation are complex, and they include the patient, primary social support (usually family), the medical practitioner, and the mental health practitioner. The support network may guide the patient toward subjective cues (by asking, "How do you feel?") without acknowledging that subjective and objective indicators of well-being may not be aligned. The segments of one's support network also may disagree on a range of issues, including the nature and consequences of the actions needed to manage the self-regulatory goals. A lack of coherence within the social system may present particular challenges for an individual who is trying to successfully navigate a self-regulatory process that includes more than one illness, and this lack of coherence ultimately may undermine an individual who is struggling with co-morbid conditions.

There are three domains (i.e., cognitive representations, behavioral responses, social functioning) where explicit attention to managing co-morbidity may lead towards productive interventions. Table 3 illustrates how these principles for intervention can be put into effect for a patient with diabetes and depression (see Example 1) as well as for a patient with co-morbid heart disease and depression (see Example 2).

Cognitive Representations

In order to facilitate management of a co-morbid condition, one's cognitive representation needs to reflect the coherence of chronic disease and depression management. In the context of either a mental health or medical condition, people are often poor mental accountants of their symptoms (Gonder-Frederick & Cox, 1991), are inaccurate in their reports of symptoms (Barsky, Cleary, Barnett, Christiansen, & Ruskin, 1994; Weinger, Jacobson, Draelos, Finkelstein, & Simonson, 1995), and are likely to under-report their symptoms (Mayne,

1999). When informed of the presence of risk, individuals tend to minimize threats to health status (Croyle, Sun, & Louie, 1993; Jemmott, Ditto, & Croyle, 1986). Ultimately, the lack of perceived seriousness of symptoms may limit engagement in health behavior such as medication adherence (Chambers, Markson, Diamond, Lasch, & Berger, 1999) or exercise (Miller, 1997). This issue is particularly important among individuals with asymptomatic conditions (e.g., hypertension) where patients mistakenly believe they can isolate specific symptoms (Baumann & Leventhal, 1985; Meyer et al., 1985).

Illness identity may facilitate disease management. Durable, central self-identities will affect behavior and shape cognitive processes over the long term (Andrews, 1989; Safran, 1990). For example, individuals who accepted that they were an asthma sufferer were much clearer in respecting their need for prophylactic medication than those individuals who did not accept the identity of an asthma sufferer (Adams, Pill, & Jones, 1997). Similarly, individuals whose cognitive representation includes specific health behaviors may be more likely to engage in these behaviors. Kendzierski & Whitaker (1997) found in a sample of 67 female undergraduates that individuals with a self-schema consistent with dieting were more likely to recover from a lapse in dieting and eventually re-engage in dieting behavior. Comparable findings have been reported among individuals whose self-schema is consistent with exercise (Kendzierski, 1990).

Viewing co-morbidity from the perspective of attainable life goals (i.e., future oriented, controllable) is critical (Czuchta & Johnson, 1998; Davidson and Strauss, 1995). Davidson and Prkachin (1997) examined the interaction of optimism, unrealistic optimism (i.e., the negation of relative risk of health problems), and health behaviors in two studies among undergraduates. In their first study, 72 participants completed measures of optimism and unrealistic optimism on the first day of class. Six weeks later, those participants completed an exercise scale. Individuals high on optimism but low on unrealistic optimism were most likely to engage in self-reported exercise. In a second study, 114 undergraduates were enrolled in a CHD prevention course. Individuals high on optimism but low on unrealistic optimism at the beginning of the course were more likely to report that they gained knowledge. Although these studies utilize undergraduates rather than patients as participants, the findings lend support to the idea that characterizing CHD as a condition that cannot be “cured,” but that can be managed or improved with behavioral regimens such as exercise (i.e., CHD is chronic yet controllable), should facilitate both improved mood and health behaviors.

Behavioral Responses

In reviewing the literature, it appears that the management of chronic disease and depression is linked by behavioral functioning (i.e., behavioral management of these conditions). A mounting body of literature suggests that engagement in behavioral activation, or events that increase pleasure and mastery, is associated with improved mood (Jacobson et al., 1996). Cognitive-behavioral therapies for depression suggest that engagement in enjoyable or mastery-oriented behaviors will improve cognition and mood (Beck et al., 1979). Although positive affect can disrupt control of chronic illness (as discussed earlier), if patients are taught to interpret improvements in mood as a sign that they are mastering their disease-related fears and enhancing their perceived control, they are likely to balance successful disease management with mood-enhancing pleasurable activities.

In working towards the goal of managing co-morbidity, it may be important to focus specifically on behavioral interventions that have demonstrated benefit to both depression and chronic physical disease. As an example, the Center for Disease Control (Pate et al., 1995) suggests that regular physical activity is part of a healthy lifestyle. In particular, exercise has generally been shown to improve disease outcomes (for a review, see Dubbert, 2002) and depression (Boule et al., 2001; Singh, Clements, & Fiatarone, 1997; Singh, Clements, &

Fiatarone-Singh, 2001). This effect appears consistent among individuals with chronic physical disease, and among coronary patients, exercise improves not only indicators of disease outcomes, but also depression (Kugler, Seelbach, and Kruskemper, 1994; Milani & Lavie, 2007). However, patients who engage in exercise must be taught to distinguish between frightening subjective cues (e.g., chest pain as a result of post-surgery healing) and objective indicators of distress (e.g., cardiac threat). If exercise leads to frightening symptoms, it can increase anxiety and depressed mood, inhibiting future activity. Only with the help of one's support network (especially one's medical doctor) can patients begin to distinguish between threatening and non-threatening symptoms, allowing for the adoption of beneficial behaviors (e.g., exercise). For example, Petrie and colleagues (2002) demonstrated that a three-session, hospital-based intervention that educated patients about the distinction between cardiac and non-cardiac symptoms (including natural but potentially frightening symptoms that may be felt during exercise) led to enhanced functional outcomes post- MI.

Social Functioning

Managing co-morbidity by enhancing social functioning and engaging the social network will facilitate more effective disease and depression management. Several theorists have suggested that social role functioning is important to long-term management of mental illness (Davidson & Strauss, 1995) as well as aging (Lemon, Bengtson, & Peterson, 1972). Disruption of valued life activities increases risk of a more general disruption of the self (Mechanic, 1995). Consistent with findings that social roles are disrupted by chronic physical conditions, e.g., diabetic neuropathy (Vileikyte et al., 2005), there is some evidence that increased focus on social role functioning improves mood. Katz and Yelin (1995) examined the relation of social role functioning and depression in a four-year longitudinal study of individuals with rheumatoid arthritis. Whereas overall functional decline was not a risk factor for the development of depressive symptoms in this sample, loss of valued activities predicted higher levels of depression at follow-up.

Further, enhanced social functioning may provide reinforcement for engaging in difficult self-management behaviors, thus limiting the associated negative affect (Keough & Markus, 1998). For example, not participating in a holiday feast will not be depressogenic if it is perceived to be compatible with another higher-order, rewarding principle (e.g., being a responsible parent and spouse). The short-term sacrifice of participation in a given social event ensures the longer-term survival of the role and functions that are required for a valued member of the family. Success in defining the self in terms of higher-order principles will require sharing goal-relevant information with family members.

Evidence also suggests that interventions that integrate spouses into diabetic care for elderly individuals are associated with improvement in metabolic control of diabetes (Gilden, Hendryx, Casia, & Singh, 1989). Others have examined an integrated social network approach for depression alone. Miller and colleagues (2005) examined whether delivering family therapy to depressed patients with poor family functioning would improve outcomes. In this study, 121 hospitalized depressed patients were grouped on the basis of their level of cognitive impairment (high, low) and family dysfunction (high, low), and then were either "matched" or "mismatched" to a treatment designed to directly address this deficit. The four treatment conditions were: a) pharmacotherapy and clinical management, b) cognitive therapy and pharmacotherapy, c) family therapy and pharmacotherapy, and d) cognitive therapy plus family therapy and pharmacotherapy. Randomized treatment began at discharge from the hospital and continued for 24 weeks on an outpatient basis. Results indicated that while treatment matching only improved short-term outcome for patients who were symptomatic at discharge from the hospital, patients who received additional family therapy had significantly better outcomes than those who did not, as indicated by a faster decrease in depressive symptoms and

significantly lower levels of symptoms at a Week 12 assessment. These advantages for patients receiving family therapy diminished slightly over time, with fewer significant differences obtained at the Week 24 assessment. However, the overall pattern of results strongly suggests that an integrated approach that adds family therapy to medical and individual treatment substantially improves the outcome for severely depressed patients, and may be useful when managing co-morbid depression and chronic physical disease.

Clinical Implications

The management of co-morbidity requires the patient to utilize a multi-level process of attending to symptoms moment-by-moment, conceptualizing effectual actions for the present and the future, and incorporating a broad, positive view of one's self (e.g., "I can see a longer term goal for me to be active and involved in family occasions, even though I have diabetes"). In order to illustrate the clinical implications of our model, consider again an individual who struggles with both depression and type 2 diabetes and who is invited regularly to social events by family, friends, and co-workers. This individual is using "existing care": two separate treatment providers with two separate goals of managing depression and diabetes. Depressed individuals often experience symptoms such as sadness, lack of pleasure in previously enjoyable activities, and reduced appetite, weight, and energy (American Psychiatric Association, 1994). Perhaps with the assistance of a mental health professional, this individual may determine that depression could be managed by actively engaging in social events, particularly those that may be festive and enjoyable (Beck et al., 1979; Jacobson et al., 1996). Attending happy hour after work, going out to dinner with friends, and joining family gatherings on the weekend potentially improve mood and facilitate specific positive goals (e.g., viewing oneself as important to others, consuming enjoyable food and thus improving appetite).

Now consider that individual from the perspective of diabetes management. If the individual is preparing to attend the same social events while attempting to manage diabetes, there is likely to be exposure to unhealthy, yet desirable, high sugar/high fat foods. Upon engaging in disease management behavior (American Diabetes Association, 2002), the individual needs to keep her glucose levels and weight stable. Therefore she will need to significantly restrict her eating, eat differently (e.g., bring her own food), or avoid the event. As a result, she may feel that disease management will deprive her of food and enjoyable life activities (Rubin & Peyrot, 2001). Further, because elaborate food preparation and consumption is central to the daily lives of many cultures, and diabetic diets often are inconsistent with culturally accepted diet patterns (Griffin, Gilliland, Perez, Upson, & Carter, 2000), she may feel that disease management will require disengagement and create feelings of social isolation, a stimulus to depressed mood.

How does an *integrated* view of disease and depression management influence the actions of an individual trying to cope with social events such as these? Current practice, which separates the two conditions (e.g., I have to manage both depression and diabetes), leads to actions that overlap in content (that is, managing social interaction and food intake), yet may conflict (e.g., attend dinner vs. not attend dinner, eat enjoyable food vs. restrict). Although a compromise, such as attending the event but eating less (or not at all), may seem ideal and easily attainable if limited in scope, these types of compromises are difficult as they recur and are likely to lead to loss of pleasure and loss of support from family and friends (Rubin & Peyrot, 2001; Sorkin, 2002). Whereas engaging in healthy behaviors may be difficult for most people (Bellg, 2003), for those with co-morbid chronic physical disease and depression, mismanagement of these self-regulation goals can be devastating. Limiting pleasurable activities, restricting food intake, and avoiding social events may exacerbate major depression, whereas increasing relaxation and enjoyment, but increasing sugar and fat intake could worsen diabetes; both outcomes increase risk for loss of functioning and for mortality.

Through the addition of a self-regulatory goal of managing co-morbidity, one's likelihood of resolving competing or conflicting actions is increased. Cognitive representations of disease and depression need to be integrated, and performance of behaviors that are synergistic with chronic disease and depression management should be encouraged. Patients need to be prepared for and aware of the possibility that management of one condition may conflict with management of the other, and they need to create an action plan for success. The plan would likely integrate elements of self-management with behaviors designed to manage the social environment, i.e., to prepare others to accept one's needs, to prepare the foods needed for disease management, and to encourage those "in the know" to act as informers and/or protective agents. Care needs to be integrated within the patient's existing social system. It is critical that patients and practitioners work together to develop a goal related to the overlap between the two conditions, focusing on representations of patient experiences and behavioral strategies (Clark & Gong, 2000). Ideally, the patient, family, medical doctor and mental health provider could meet to discuss issues related to how to best navigate challenging events such as dinners at friends' houses and gatherings with family members, thus minimizing contradictory messages from the various members of the treatment team.

Finally, the patient must work to foster a positive self-view as related to the management of the co-morbid conditions by looking beyond the particular actions (e.g., food choices) or events (e.g., a family celebration). That is, the patient, her practitioners, and her support system may want to identify long-term goals, such as being healthy enough to be an active spouse, parent and grandparent. Therefore, when the patient chooses a strategy to help manage the situation (e.g., bringing her own food to an event, saying she is a vegetarian, taking a stroll after eating) the forethought and energy she expends can be reconstrued as time invested in living a long, healthy life; and rather than being offended that their food is not good enough, family and friends can recognize that their loved one's food choices are wise and that positive regard for and encouragement of the patient's healthy behavior will help to enhance her positive mood.

Discussion

This review highlights the inconsistent findings from studies examining whether treating depression improves disease outcomes and whether chronic disease management improves depressed mood. We propose that disease management may contribute to the underregulation and misregulation of depression management and vice versa. When individuals attempt to manage one aspect of their co-morbid condition, they may assign too much priority to these particular self-regulatory goals, thus interfering with or undermining goals related to the other condition. Given the lack of integration of disease and depression management, it is not surprising that patients lack the understanding needed to prioritize self-regulatory goals in a way that makes disease and depression management synergistic. The theoretical framework presented in the current paper describes how depression treatments and chronic disease management programs may be conceptually integrated. To resolve failures in self-regulation, patients should consider management of co-morbidity as an additional self-regulatory goal, allowing for open discussion (among patients, practitioners and researchers) of actions that are likely to improve both depression and chronic physical disease. Clinical outcomes will likely improve once depression treatment and chronic disease management are better integrated.

The roles of cognition, behavior, and social functioning in understanding and managing co-morbid depression and chronic physical disease must receive close attention. Managing either condition involves behavioral processes, including medication adherence, diet, exercise, and self-monitoring. For the purpose of the current paper, studies investigating the effect of psychosocial interventions such as behavior therapy or stress management on disease outcome were not included, because such programs are highly overlapping with empirically supported treatments for depression. Nonetheless, it is important to acknowledge that others have

demonstrated the utility of such interventions in managing risk factors and symptoms related to cancer (Penedo, 2006), CHD (Blumenthal et al., 2002), HIV/AIDS (Antoni et al., 2006), and diabetes (the Diabetes Prevention Program Research Group, 2005), for example. The importance of managing stress and negative mood among individuals with chronic illnesses is evidenced by clinical interventions such as these, yet a consensus from randomized controlled trials of psychosocial programs' overall effect on morbidity and mortality is lacking (Fekete, Antoni, & Schneiderman, 2007; Goldston & Baillie, 2008). Perhaps due to the numerous biological mechanisms linking disease and depression, most models of co-morbidity have focused on biological factors, and medication treatment trials far exceed psychosocial intervention trials. A coordinated approach to managing behavioral processes in the context of co-morbid depression is essential, and improved treatment of co-morbid conditions will fail to be effective without a direct focus on these processes.

Although the current paper has focused on major depressive disorder, some of the issues related to managing co-morbidity may not be specific to depression. For example, researchers have explored the challenges associated with managing schizophrenia in the context of co-morbid medical illnesses (e.g., Lambert, Velakoulis, & Pantelis, 2003), giving particular attention to the management of important factors such as cigarette smoking, diet and exercise, unsafe sexual behavior, and medication side effects (Green et al., 2003). Anxiety disorders also frequently co-occur with medical illnesses, and a recent review by Roy-Byrne and colleagues (2008) argues that anxiety disorders may play as important of a role in morbidity and mortality as depression. Indeed, it is possible that one of the ways that disease and depression influence each other is through their mutual effect on anxiety. For example, many of the effects of negative affect on awareness of symptoms may be the result of anxiety, rather than depression (Leventhal, Hansell, Diefenbach, Leventhal, & Glass, 1996). Similarly, increased health care consumption may be the result of anxiety rather than depressed mood (Strik et al., 2004). And as Barlow (1991) has suggested, anxiety specific to health threats may be a critical precursor of depression in response to the occurrence, recurrence and/or worsening of physical disease.

As this is a broad, multi-faceted field, several important issues were beyond the scope of the current review. First, chronic physical disease and depression were conceptualized throughout the paper as separate entities, and the term "co-morbid" was used to describe individuals suffering from both conditions. This is in contrast to previous illness cognition models that assume emotional reactions (e.g., depressed mood) are directly linked to the presence of disease (Leventhal et al., 1992). The possible causes for depression are too numerous to assume etiology, and regardless of etiology, the presence of major depression may result in its own set of biological, cognitive and behavioral processes that perpetuate disease. Resolution of these issues ultimately will have important implications for how chronic disease and depression are conceptualized and treated. Second, some otherwise complex processes have been simplified, and the set of self-regulatory goals we propose is incomplete. For example, the potential benefit of depression treatment on adherence is highlighted, as though strict adherence is always associated with improved outcome. However, this may not always be the case (Hays et al., 1994; Petrie et al., 2002).

Third, the current review focuses primarily on cognitive, behavioral, and social processes. The complex biological processes that may underlie the link between co-morbid conditions and the issues related to the pharmacologic management of disease and depression were beyond the scope of this paper. For example, it is possible that some of the effects of medications aiming to improve the depressive disorder may exacerbate disease symptoms and vice versa (e.g., Norra, Skobel, Arndt, & Schauerte, 2008). Reviews and ongoing research focusing on the biological bases of the relationships between depression and disease are crucial (Krishnan et al., 2002; Skala, Freedland, & Carney, 2006), and our limited discussion of these issues in no way reflects our estimation of its importance.

Finally, we do not intend to suggest that treating both depression and physical disease as separate entities is not worthwhile. On the contrary, managing depression is an important avenue to overall disease management and vice versa. Assuming that the cumulative effects of treating one condition in isolation are not harmful, treating both conditions as unique and separable is not only important to do, but inevitable. Medical doctors need not become experts in depression management, and therapists need not become experts in disease management. Instead, practitioners and researchers should communicate with specialists in different fields, with the goal of identifying areas of overlap. Providers of care must be unambiguous in describing their own and other practitioners' goals in order to help patients identify the ways in which their self-regulatory goals are interrelated. Integration of the treatment system will bolster patients' abilities to identify and manage their own self-regulatory goals, ultimately leading to better physical and mental health outcomes.

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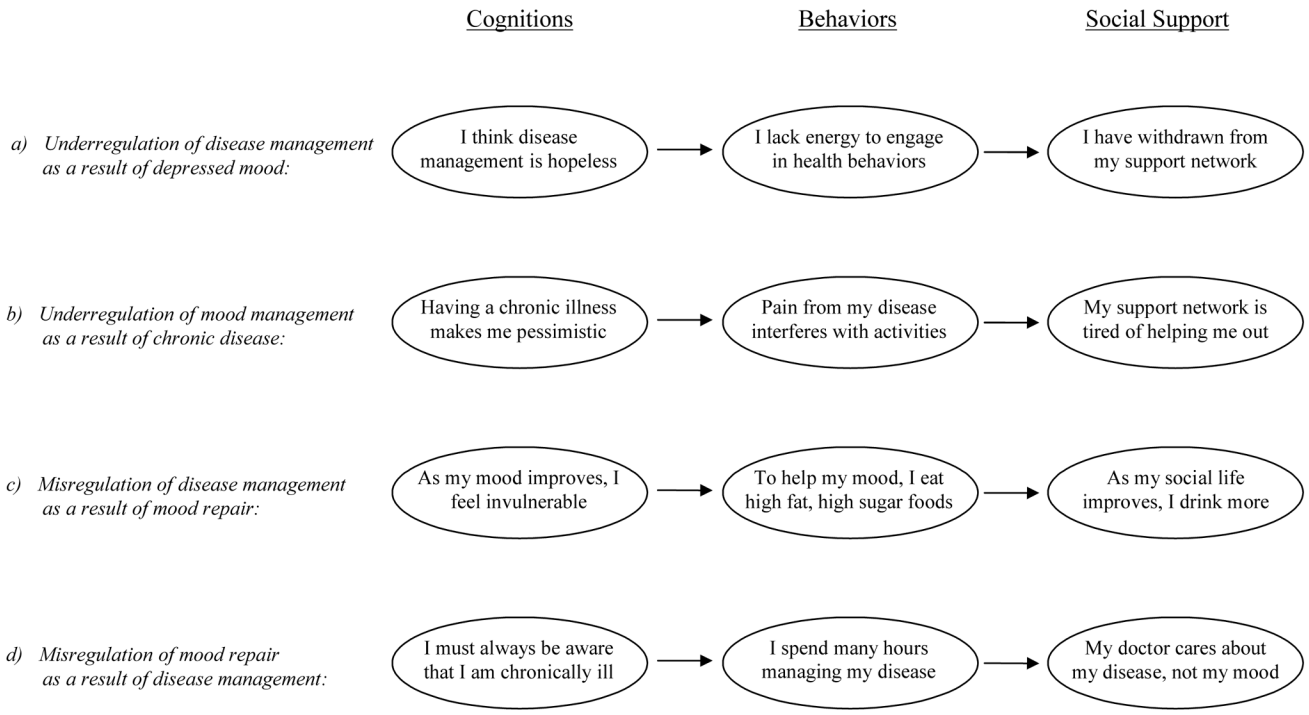

Figure 1.
Pathways for underregulation and misregulation for an individual with co-morbid disease and depression

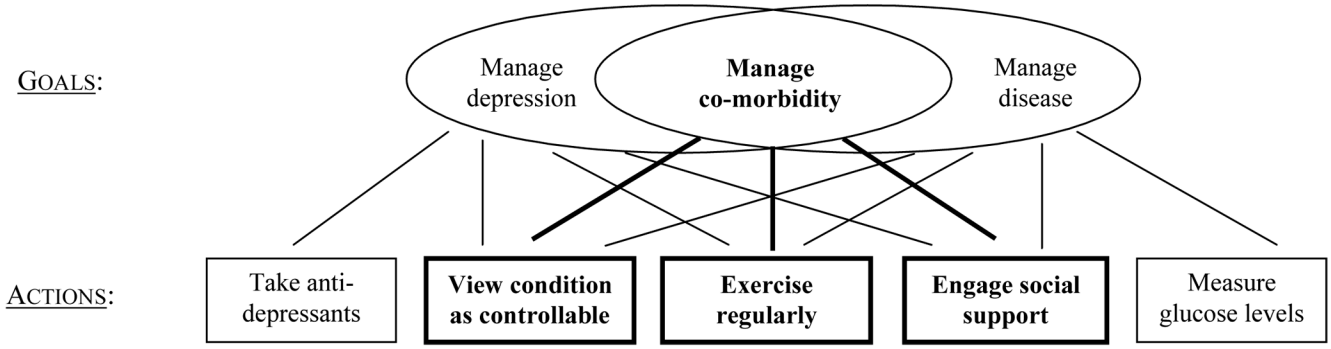

Figure 2.
Three self-regulatory goals and associated actions for individuals with co-morbid depression and chronic physical disease

Table 1

Randomized controlled trials examining the effects of depression treatment on disease outcomes

Disease	Authors	# Subjects	Time	Treatment	Control Condition	Outcome Measure for Depression	Outcome Measure for Disease
Coronary Heart Disease	Berkman et al. (2003)	1332	24 weeks 2 year follow-up	CBT	Usual Care	+ BDI + HRSD	= Mortality
	Glassman et al., (2003)/ Serebruany et al., (2003)	369	24 weeks	Sertraline	Placebo	=HRSD	= Mortality + platelet activation
	Strik et al., (2000)	54	9 weeks	Fluoxetine	Placebo	= HRSD	= Cardiac Events
	van Melle et al., (2007)	331	18 months	Mirtazapine or Citalopram or psychotherapy	Usual Care	= BDI = ICD-10	= Cardiac Events
Diabetes	Katon et al., (2004)	329	12 months	Antidepressant or psychotherapy	Usual Care	+ SCL-90	= Glycemin control
	Lustman et al., (2000)	60	8 weeks	Fluoxetine	Placebo	+ BDI + HRSD	= Glycemic control
	Lustman et al., (1998)	51	10 weeks 6-month follow-up	CBT	Diabetes Education Program	+ BDI	= Glycemic control + at follow-up
	Lustman et al., (1997)	68	8 weeks	Nortriptyline	Placebo	+ BDI	= Glycemic control
HIV	Elliot et al., (1998)	75	12 weeks	Paroxetine or Imipramine	Placebo	+ HRSD	= CD4 cell count
	Rabkin et al., (1999)	120	8 weeks	Fluoxetine	Placebo	+ HRSD count	= CD4 cell
	Rabkin et al., (1994)	97	6 weeks	Imipramine	Placebo	+ HRSD	= CD4 cell count

[a] "+" = Depression treatment improved outcome; "=" = no difference; "–" = Depression treatment worsened outcome

HRSD = Hamilton Rating Scale for Depression; CBT = Cognitive Behavioral Therapy; BDI = Beck Depression Inventory; ICD-10 = International Statistical Classification of Diseases and Related Health Problems, Depressive Disorder; SCL-90 = Hopkins Symptoms Checklist-90 depression score; MI = Myocardial Infarction

Table 2

Randomized controlled trials of the effects of disease management on depression

Disease	Authors	# Subjects	Time	Treatment	Control Condition	Outcome Measure for Depression
Coronary Heart Disease	Horlick et al., (1984)	116	6 week intervention 24 week follow-up	Education/Group Discussion	Usual Care	= MMPI
Congestive Heart Failure	Rogers et al., 1994	5,025	2 years	Enalapril	Placebo	= POMS
Hypertension	Perez-Stable et al., (2000)	312	52 weeks	Propanolol	Placebo	= CESD, BDI
Diabetes						
	Piette et al., (2000)	240	52 weeks	ATDM	Usual Care	+ CESD
	Wing et al., (1986)	50	12 week intervention follow-up at 48 weeks	Behavioral Weight Control + Glucose Self-	Standard Behavioral Weight Control	+ BDI
Arthritis						
	Lorig et al., (1999)	331	6 week intervention 4 month followup	ASMP	Wait List	= CESD
	Barlow et al., (2000)	240	6-weeks 4 month follow up	ASMP	Wait List	+HADS
Cancer	McQuellon et al., (1998)	180	1 day	Orientation Intervention	Usual Care	+ POMS, CESD

"+" = Depression treatment improved outcome; "=" = no difference

HRSD = Hamilton Rating Scale for Depression; BDI = Beck Depression Inventory; POMS = Profile of Mood States; MMPI = Minnesota Multiphasic Personality Inventory; CESD = Center for Epidemiologic Depression Scale; HADS = Hospital Anxiety and Depression Scale; ASMP = Arthritis Self-Management Program; ATDM = Automated telephone disease management.

Table 3

Interventions for co-morbid depression and chronic physical disease

Principles for Intervention	**Example 1: *Diabetes and Depression***	**Example 2: *Heart Disease and Depression***
Integrate disease and depression management by recognizing that the physical illness and mood disorder influence one another.	*Recognize that depression can exacerbate diabetes; In the winter months, depression may worsen and make diabetes harder to manage.*	*Recognize that CHD may heighten depression; Heart attack risk may increase stress, which can worsen depression.*
Cognitive Representations: Identify and modify maladaptive disease cognitions.	*Reduce self-blame for onset of diabetes; modify time course as chronic but controllable.*	*Reduce catastrophizing about potential consequences of returning to work after a heart attack; increase sense of personal control.*
Behavioral Responses: Link behavioral functioning and engage in behaviors that perpetuate better self-regulation of both conditions.	*Become aware that managing diabetes can be depressing; Incorporate pleasurable activities into one's daily routine to counterbalance this.*	*Become aware that depression reduces one's motivation to engage in activities that control disease; Recognize the multiple benefits of exercise.*
Social Functioning: Enlist the aid of one's social network in adopting coping responses consistent with both conditions.	*Encourage family members to have celebratory dinners, but also to include healthy food choices.*	*Arrange for a conference call with one's physician, psychologist, and spouse to discuss reasonable treatment-related goals.*