



Research report

Depression and vulnerability to incident physical illness across 10 years

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ABSTRACT

Background: While considerable research exists on the role of physical illness in initiating depressive reactions, the role of depression in the onset of physical illness is much less studied. Moreover, whereas almost all previous research on depression and incident physical illness has involved specific physical illnesses, the present study examines the link between depression and incident physical illness more generally.

Methods: The study followed 388 clinically depressed patients who were entering treatment for unipolar depressive disorders and 404 matched community controls across 10 years. In self-report surveys, sociodemographic and health behavior data were indexed at baseline and physician-diagnosed medical conditions were indexed at baseline and at 1, 4, and 10 years during the follow-up period.

Results: After accounting for prior physical illness and key demographic and health behavior factors, membership in the depressed group was significantly linked to physical illness during the follow-up period. In these prospective analyses, depressed patients showed an almost two-thirds higher likelihood of experiencing physical illness during the follow-up period compared to community controls. The prospective association between depression and subsequent physical illness was evident for both less serious and more serious physical illness.

Limitations: Although participants were asked to report only physician-diagnosed conditions, the association between depression and physical illness may have been due to depressed individuals perceiving themselves as more ill than they were.

Conclusions: The World Health Organization has included the co-morbidity between depression and chronic physical illness among its ten concerns in global public health. The current findings broaden the growing awareness of the co-morbidity between depression and physical illness to encompass a vulnerability of depressed individuals to physical illness more generally.

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1. Introduction

The role of physical illness in predicting depression is well-established across a wide spectrum of illnesses. For example, severe, potentially life-threatening illnesses, including heart disease (Holahan et al., 1995), stroke (Robinson, 2003), and

cancer (Massie, 2004), are associated with depression. In addition, patients dealing with chronic pain-inducing illnesses, such as back pain (Currie and Wang, 2004), arthritis (Keefe et al., 2002), and migraine (Breslau et al., 2003), are vulnerable to depression. However, while considerable research exists on the role of physical illness in initiating depressive reactions, the reverse process—the role of depression in the onset of physical illness—is much less studied (Farmer et al., 2008; Patten et al., 2008). Yet, this topic is central to the quality of life of depressed individuals and, more broadly, to medical care and to reducing the illness burden on society (Evans et al., 2005). The purpose of

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the present study was to investigate the prospective relationship between depression and a wide spectrum of physical illnesses across a 10-year period.

1.1. Depression as a predictor of physical illness

Accumulating evidence suggests that depression may increase morbidity and mortality from physical illness (Stover et al., 2003). Evidence for the role of depression in predicting physical illness can be divided into two lines of inquiry. Most research has examined the role of depression in illness course, recovery, and relapse among individuals with existing specific physical illnesses. More recently, however, the investigative focus has broadened to include the role depression plays in predicting the onset of new illnesses among previously healthy individuals. Almost all of this more recent work has focused on depression as a predictor of specific physical illnesses. However, interest is now emerging in the potential predictive role of depression in incident physical illness more generally.

1.2. Depression and the course of specific physical illnesses

Although depression has been found to predict the course of many physical illnesses, the strongest evidence pertains to heart-related illnesses and, secondarily, to chronic pain. For example, among patients with coronary artery disease followed for from 1 to 20 years, both major depression (Carney et al., 1988) and depressive symptoms (Whooley et al., 2008) are positively associated with adverse cardiac events, including myocardial infarction and cardiac-related mortality. Moreover, considerable evidence indicates that major depression (Frasure-Smith et al., 1993) and depressive symptoms (Ahern et al., 1990; Frasure-Smith et al., 1995; Welin et al., 2000), including low levels of depressive symptoms (Bush et al., 2001) are associated with an increased risk of mortality after myocardial infarction.

Further, both major depression (Connerney et al., 2001) and depressive symptoms (Burg et al., 2003; Contrada et al., 2008; Jenkins et al., 1996) are positively associated with poorer recovery, including less symptom relief and a higher likelihood of cardiac-related rehospitalization in patients recovering from heart, primarily coronary artery bypass, surgery. Major depression is also associated with more intense and longer lasting pain and greater and longer-term disability among chronic pain patients, including patients with diffuse pain at multiple sites (Ericsson et al., 2002), chronic (primarily low back) pain (Bair et al., 2003), and rheumatoid arthritis, (Dickens et al., 2002; Lowe et al., 2004).

1.3. Depression and the onset of specific physical illnesses

More recent work suggests that depression is a predictor of specific physical illnesses in initially healthy individuals. Again, evidence is especially clear with heart-related illnesses and, secondarily, chronic pain. Two independent reviews found that the relative risk for the onset of coronary heart disease was 1.64 for depressed compared to non-depressed individuals followed for an average of 13 years (Rugulies, 2002; Wulsin and Singal, 2003). For example, studies that have followed large population samples for from 4 to 10 years have found that both major depression (Surtees et al., 2008) and depressive symptoms (Ferketich et al., 2000; Marzari et al., 2005) predict incident

coronary heart disease in individuals initially free of heart conditions, controlling for common risk factors. There is also evidence that major depression is associated with a marginally increased risk for incident hypertension (Meyer et al., 2004).

Depressed patients are also more likely to report unexplained pain than non-depressed patients. For example, population-based studies have reported links between major depression and incident chronic back pain (Currie and Wang, 2005; Larson et al., 2004) and between depressive symptoms and incident arthritis (Seavey et al., 2003). Further, both major depression (Eaton et al., 1996) and depressive symptoms (Engum, 2007; Golden et al., 2008) have been linked to incident type 2 diabetes in large samples followed for from 3 to 10 years. There is also some evidence from a large sample followed for more than 10 years that depressive symptoms may predict incident ischemic stroke (Arbelaez et al., 2007).

1.4. Depression and the onset of physical illness more generally

Very recently, research on the role of depression as a risk factor for incident physical illness has expanded from a focus on specific physical illnesses to encompass physical illness more generally. For instance, after an extensive literature review, Evans et al. (2005) concluded that the evidence suggests a potential for depression as a risk factor for incident physical illness across a spectrum of illnesses. However, the authors also noted inconsistencies in the literature on depression and incident physical illness and called for additional prospective studies.

Three recent empirical studies offer further support for a potential link between depression and incident physical illness more generally. Farmer et al. (2008) retrospectively examined the concordance between lifetime histories of recurrent depression and several physical health diagnoses among over 1500 individuals with recurrent depression and almost 900 controls in the United Kingdom. The authors found higher rates of reported physical illnesses, including myocardial infarction, liver disease, gastric ulcer, osteoarthritis, and rheumatoid arthritis, among depressed individuals compared to psychiatrically healthy controls.

In addition, McCusker et al. (2007) prospectively followed over 200 older medical patients for 1 year. The investigators found that, controlling for prior illness, major depression prospectively predicted poorer subsequent physical health status on the Medical Outcome Study Short Form Health Survey (SF-36). Further, Patten et al. (2008) prospectively followed over 15,000 adults in the Canadian National Population Health Survey for up to 8 years. Controlling for prior illness, the authors reported higher rates of several chronic physical illnesses, including heart disease, hypertension, asthma, chronic bronchitis/emphysema, arthritis/rheumatism, back problems, and migraine, among individuals with major depression compared to those without major depression.

1.5. Present study

The present study extends previous research on depression and physical illness by examining the role of depression as a vulnerability factor for incident physical illness in a prospective

design controlling for prior medical conditions. Based on the few available studies on depression and physical illness more generally (Farmer et al., 2008; McCusker et al., 2007; Patten et al., 2008), it was hypothesized that, controlling for prior medical conditions, depression would prospectively predict the likelihood of experiencing new medical illnesses across a 10-year follow-up period.

The present study followed 388 clinically depressed patients and 404 matched community controls across 10 years to examine the prospective link between depression and physical illness. The data are part of a longitudinal project examining the long-term course of unipolar depression. Earlier research on the 10-year follow-up of these samples has examined life context factors in depression remission and relapse (Cronkite et al., 1998; Holahan et al., 2000; Moos et al., 1998) and the role of avoidance coping in predicting drinking behavior (Holahan et al., 2003, 2004). No previous research with this database has focused on depression and vulnerability to physical illness.

2. Methods

2.1. Sample selection and characteristics

Two samples of adults (age 18 or older) were selected: a sample of depressed patients who were entering treatment for unipolar depressive disorders and a sample of community controls who were matched with the patients in terms of area of residence and marital status (for more information on these samples, see Cronkite et al., 1998; Moos et al., 1998). Sociodemographic and health behavior data were indexed at baseline and medical conditions were indexed at baseline and at 1, 4, and 10 years during the follow-up period. Drop-outs over the 10 years were minimized by rigorously maintaining contact information, and systematically following participants through mail, telephone, and personal contacts.

2.1.1. Depressed patient sample

A sample of 424 depressed patients was selected from depressed persons in the San Francisco Bay Area who began new treatment at one of five health care facilities. The treatment facilities represented a broad range of public and private settings, including two community mental health centers, a Department of Veterans Affairs medical center, a health maintenance organization, and a private university hospital. All patients had a clinically significant unipolar depressive disorder according to the Research Diagnostic Criteria for depression (RDC; Spitzer et al., 1975). Diagnostic information was obtained by trained research staff, who used specifically designed checklists for psychiatric symptoms in the RDC in reviewing clinicians' intake and treatment records from the current and prior treatment episodes. In those cases where information on symptoms could not be determined from records (approximately 15% of cases), treatment staff members were consulted or the patient was interviewed by research staff.

Because the depressed patient sample was initially selected to study primary unipolar depression, several exclusion criteria were used at baseline. On the basis of a chart review, patients were excluded if they had a current diagnosis of alcoholism (or if significant alcohol abuse was noted in the past 6 months) or if

they had current neuropsychological, metabolic, or manic diagnoses. Depressed patients were contacted initially at the treatment facility. Of the patients contacted at baseline, 92% agreed to participate and 81% of these ($N = 424$) provided data. The participation rate for surviving depressed patients averaged 90% at each of the 3 follow-up assessments.

Among the 424 depressed patients, 388 respondents (92%) provided sufficient data for at least one follow-up assessment to be included in the prospective analyses. The present sample of 388 patients included in the prospective analyses was comprised of 220 women (57%) and 168 men (43%), and the mean age of respondents at baseline was 40 years ($SD = 13.9$; range = 18–83 years). A total of 44% of respondents were married. The ethnic distribution of the sample was 86% Caucasian, 3% Hispanic, 3% African American, 2% Asian, and 6% other ethnic backgrounds.

2.1.2. Community control sample

A sample of 424 community controls was matched demographically with the patients in terms of area of residence and marital status. The community sample was selected by a procedure in which a household was sampled randomly from the same census tract and within a 12-square-block area surrounding a matched patient's block. A new household was randomly selected if the household did not match the patient's marital status. Community controls were contacted initially by telephone. Of the individuals contacted at baseline, 87% agreed to participate and 84% of these ($N = 424$) provided data. The participation rate for surviving community controls averaged 95% at each of the 3 follow-up assessments.

Among the 424 community controls, 404 respondents (95%) provided sufficient data for at least one follow-up assessment to be included in the prospective analyses. The present sample of 404 community participants included in the prospective analyses was comprised of 221 women (55%) and 183 men (45%), and the mean age of respondents at baseline was 39 years ($SD = 15.4$; range = 18–88 years). A total of 43% of respondents were married. The ethnic distribution of the sample was 89% Caucasian, 3% Hispanic, 2% African American, 3% Asian, and 3% other ethnic backgrounds.

2.2. Measures

Detailed descriptive and psychometric information on the measures is available in the *Health and Daily Living Form (HDL; Moos et al., 1992)*. The HDL is similar to other commonly used indexes and relates empirically to other variables and to health outcomes in expected ways. For examples of studies using the HDL, see Cronkite et al. (1998), Holahan et al. (2000); Holahan et al. (2003, 2004), and Moos et al. (1998).

2.2.1. Depression

Depression at baseline was indexed by group membership in the community control sample (score = 0) versus the depressed patient sample (score = 1). We used a measure of depressive symptoms at baseline as an additional way to validate group status. Depressive symptoms were tapped by an index of 18 symptoms experienced during the previous month, derived from the Research Diagnostic Criteria (Spitzer et al., 1975). Examples of items are "feeling depressed (sad or

blue)” and “feeling guilty, worthless, or down on yourself.” Responses are on a 5-point scale reflecting how frequently symptoms were experienced, from never (0) to often (4). The depressive symptoms score is the sum of responses across the 18 items (Cronbach’s $\alpha = .92$). Among participants in the prospective analyses, depressed patients and community controls differed significantly on depressive symptoms at baseline ($F(1, 789) = 667.47, p < .01$), with depressive symptoms for depressed patients ($M = 43.74, SD = 14.83$) more than twice as high as those for community controls ($M = 19.20, SD = 11.76$).

2.2.2. Health behaviors

We controlled for three health behaviors, which were indexed at baseline: tobacco smoking, drinking problems, and physical activity. *Tobacco smoking* was operationalized as responding no (score = 0) versus yes (score = 1) to an item asking whether the respondent currently smoked tobacco (cigarettes, cigars, or pipe). Following Brennan et al. (2005), *drinking problems* were operationalized as the absence (score = 0) versus presence (score = 1) of one or more drinking problems from a list of 8 problems experienced in the past year because of “too much drinking” (e.g., problems with one’s job or family arguments). The drinking problems measure is positively related to other indexes of severity of drinking problems, such as alcohol consumption, days intoxicated, and dependence symptoms (Finney and Moos, 1995). Following Harris et al. (2006), *physical activity* was indexed by summing four items asking patients whether or not (no = 0; yes = 1) they engaged in: (a) swimming or tennis with friends, (b) or family, or (c) long hikes or walks with friends (d) or family during the last month. The total score ranged from zero (no activity) to four (high activity).

2.2.3. Financial resources

Because financial resources are associated with a lower likelihood of physical illness (Adler et al., 1999), we also controlled for financial resources. At baseline, respondents were asked to report their own annual earnings before taxes (wages, salary, commissions) and whether or not they were currently employed either part or full time. We indexed financial resources as a participant’s earnings at baseline or, when earnings were not provided (63 cases), by substituting employment status at baseline, using standard scores for both measures to equate their scales.

2.2.4. Physical illness

Medical conditions were indexed at each assessment by asking participants to indicate whether they had experienced any of 14 medical conditions during the previous 12 months. Participants were instructed to report a medical condition “only if diagnosed by a physician.” For each medical condition, respondents indicated whether they had experienced the condition by responding “no” (score = 0) or “yes” (score = 1). A composite measure of physical illness at baseline was operationalized as the absence (score = 0) versus presence (score = 1) of one or more medical conditions at baseline. Similarly, a composite measure of physical illness during the follow-up period was operationalized as the absence versus presence of one or more medical conditions

during the follow-up period when data were available for at least one follow-up assessment.¹

In additional analyses, we divided the medical conditions at the median into less serious and more serious physical illness based on the Seriousness of Illness Rating Scale (Wyler et al., 1968; Rosenberg et al., 1987), using the same strategy to operationalize the absence versus presence of one or more medical conditions within each domain. The 14 medical conditions, ranked in order of increasing illness seriousness, were: bronchitis, serious back trouble, anemia, asthma, kidney trouble, arthritis or rheumatism, high blood pressure, ulcer, tuberculosis, diabetes, chronic liver trouble, heart trouble, stroke, and cancer. Less serious physical illness encompassed bronchitis through high blood pressure, and more serious physical illness encompassed ulcer through cancer.

The procedure of indexing respondents’ self-reported but professionally-diagnosed physical illnesses is used in the U.S. Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System (CDC, 2009). Several studies have assessed the validity of this procedure by comparing patients’ self-reports with medical data for a range of medical conditions, including asthma, arthritis, high blood pressure, diabetes, and cardiovascular disease, and have reported acceptable to high levels of agreement (Barlow et al., 1998; Farmer et al., 2008; Holahan et al., 1995; Martin et al., 2000).

To assess the criterion-related validity of the measure of physical illness in the present study, we used more serious physical illness across the full study period to predict mortality in a multiple logistic regression analysis, controlling for age. Mortality was indexed by public use Social Security and National Death Indexes. Based on death certificates, we excluded nine cases of suicide, all of which involved depressed patients.² Controlling for age, more serious physical illness during the study period was significantly associated with higher mortality ($OR (N = 791) = 3.10, p < .01, 95\% CI = 1.68, 5.69$), with participants reporting a serious medical condition more than three times more likely to die during the study period.

3. Results

3.1. Tests of potential of control variables

In developing the logistic regression models, we examined six potential control variables (sex, age, tobacco smoking, drinking problems, physical activity, and financial resources) among participants included in the prospective analyses ($N = 792$). Table 1 shows group comparisons on the potential control variables at baseline for depressed patients and community controls. Depressed patients and community controls did not differ significantly on sex or age. However, at baseline, the depressed patients reported higher rates of tobacco smoking and drinking problems and had lower physical activity and financial resources than did community controls. Sex was not associated with physical illness during the follow-up period ($\chi^2(1, N = 792) = 1.70, p = .19$). Age

¹ Results using a binary index of one or more medical conditions versus a continuous measure of the number of medical conditions were essentially the same.

² Results including cases of suicide were similar to the reported results.

Table 1

Group comparisons on potential control variables at baseline for depressed patients ($n=388$) and community controls ($n=404$).

Variable	Depressed patients	Community controls	Statistical test ^a
Sex			$\chi^2=0.32$
Female	220 (57%)	221 (55%)	
Male	168 (43%)	183 (45%)	
Age	39.75 (13.93)	39.19 (15.43)	$F=0.29$
Financial resources ^b	-0.26 (0.88)	0.21 (1.06)	$F=45.76^*$
Physical activity (scaled 0–4)	0.95 (1.10)	1.43 (1.33)	$F=30.26^*$
Tobacco smoking (no = 0; yes = 1)	193 (50%)	136 (34%)	$\chi^2=21.07^*$
Drinking problems (no = 0; yes = 1)	43 (11%)	24 (6%)	$\chi^2=6.76^*$

Means and standard deviations (in parentheses) are shown for continuous variables; number of participants and percent (in parentheses) are shown for binary variables.

* $p<.01$.

^a df for $F=1, 790$; df for $\chi^2=1$.

^b Standardized scale.

was associated with a higher rate of physical illness during the follow-up period ($r=.27, p<.01$). In addition, higher rates of tobacco smoking ($\chi^2(1, N=792)=5.61, p<.05$) and more drinking problems ($\chi^2(1, N=792)=5.01, p<.05$) and lower physical activity ($r=-.08, p<.05$) and lower financial resources ($r=-.15, p<.01$) at baseline were associated with higher rates of physical illness during the follow-up period. Thus, age, tobacco smoking, drinking problems, physical activity, and financial resources were retained in the model as control variables.³

3.2. Preliminary cross-sectional analyses

As background, we examined the cross-sectional association between depression and physical illness at baseline among participants included in the prospective analyses ($N=792$). Specifically, we examined the association between depression-control status and physical illness at baseline in a multiple logistic regression analysis, controlling for age, tobacco smoking, drinking problems, physical activity, and financial resources. After accounting for the effects of the control variables, depression was significantly linked to physical illness at baseline ($OR=2.21, p<.01, 95\% CI=1.60, 3.06$), with depressed patients showing more than two times higher likelihood of experiencing a physical illness at baseline compared to community controls. Moreover, controlling for age, tobacco smoking, drinking problems, physical activity, and financial resources, depression was significantly linked to physical illness at baseline for both less serious ($OR=1.94, p<.01, 95\% CI=1.40, 2.68$) and more serious ($OR=4.71, p<.01, 95\% CI=2.67, 8.29$) physical illness.

3.3. Prospective analyses

Next, we tested the prospective association between depression-control status at baseline and physical illness during the follow-up period in a hierarchical multiple logistic

Table 2

Results of hierarchical multiple logistic regression analysis at each step using baseline factors to predict physical illness across the follow-up period ($n=792$).

Step	Predictors at baseline	χ^2	df
1	Prior physical illness	204.40*	1
2	Age (10-year increments)	21.09*	1
3	Additional control variables ^a	12.61**	4
4	Depression	7.78*	1

Each step controls for variables entered at all prior steps.

* $p<.01$.

** $p<.05$.

^a Tobacco Smoking, Drinking Problems, Physical Activity, Financial Resources.

regression analysis ($n=792$). At step 1, baseline physical illness entered the model. At step 2, age entered the model. To facilitate interpretation, age was indexed in 10-year increments. At step 3, the additional baseline control variables of tobacco smoking, drinking problems, physical activity, and financial resources entered the model. At step 4, depression-control status at baseline entered the model.

The results of the multiple logistic regression analysis at each step are summarized in Table 2. Each step controls for variables entered at all prior steps. Table 3 shows results of the multiple logistic regression analysis at the last step for each of the separate predictors. At the last step, after accounting for the effects of all control variables, including prior physical illness, membership in the depressed group was significantly linked to physical illness during the follow-up period, with depressed patients showing two-thirds higher likelihood of experiencing a physical illness during the follow-up period compared to community controls. Moreover, the prospective link between baseline depression and physical illness during the follow-up period, after accounting for the effects of all control variables, including prior physical illness, was evident for both less serious ($OR=1.51, p<.05, 95\% CI=1.07, 2.13$) and more serious ($OR=1.64, p<.05, 95\% CI=1.12, 2.40$) physical illness.

We also examined possible moderation of the depression-physical illness effect by age, gender, tobacco smoking, drinking problems, physical activity, or financial resources.

Table 3

Results of hierarchical multiple logistic regression analysis at the last step for each of the separate predictors of physical illness across the follow-up period ($n=792$).

Predictor	Odds ratio	95% CI
Prior physical illness (no = 0; yes = 1)	10.14*	6.40, 16.08
Age (10-year increments)	1.39*	1.21, 1.60
Financial resources ^a	0.83**	0.70, 0.99
Physical activity (scaled 0–4)	1.03	0.90, 1.19
Tobacco smoking (no = 0; yes = 1)	1.27	0.89, 1.82
Drinking problems (no = 0; yes = 1)	1.49	0.75, 2.97
Depression (no = 0; yes = 1)	1.68*	1.17, 2.42

* $p<.01$.

** $p<.05$.

^a Standardized scale.

³ Results including sex in the model were similar to the reported results.

Including interaction terms with depression for each of these factors along with all other control variables in separate multiple logistic regression analyses revealed no effects for moderation of the depression effect in predicting physical illness during the follow-up period. That is, the prospective relationship between depression and physical illness did not vary ($p > .05$) as a function of age, gender, tobacco smoking, drinking problems, physical activity, or financial resources. In comparable multiple logistic regression analyses, the prospective relationship between depression and both less serious and more serious physical illness also did not vary ($p > .05$) as a function of any of the aforementioned control variables.

We also conducted case-wise chi square analyses to examine the prospective association between depression at baseline and each medical condition across the follow-up period, restricting the analyses to individuals who reported no physical illness at baseline. Because only one case of tuberculosis was reported during the follow-up period, tuberculosis was not included in this set of analyses. A significant ($p < .05$) prospective association between depression and physical illness was evident for 6 of the 13 remaining medical conditions ($n = 467$, $df = 1$): serious back trouble ($\chi^2 = 6.08$), anemia ($\chi^2 = 13.06$), kidney trouble ($\chi^2 = 4.66$), arthritis ($\chi^2 = 6.51$), chronic liver trouble ($\chi^2 = 6.10$), and heart trouble ($\chi^2 = 4.50$). In addition, the prospective association between depression and high blood pressure showed a statistical trend ($\chi^2 = 3.20$, $p < .08$).

4. Discussion

The present study followed 388 clinically depressed patients and 404 matched community controls across 10 years to examine the prospective link between depression and physical illness. After accounting for the effects of prior physical illness, as well as of key demographic and health behavior factors, membership in the depressed group was significantly linked to physical illness during the follow-up period. Previous research on the co-morbidity between depression and physical illness has been concerned overwhelmingly with medical illness as a predictor of depressive reactions, and the potential role of depression in predicting incident physical illness is much less studied (Farmer et al., 2008; Patten et al., 2008). Moreover, almost all previous research on depression and incident physical illness has involved specific physical illnesses (for reviews, see Knol et al., 2006; Rugulies, 2002; Wulsin and Singal, 2003). This study extends previous research by examining the prospective link between depression and incident physical illness more generally.

The present findings are consistent with the few available studies on depression and incident physical illness more generally (Farmer et al., 2008; McCusker et al., 2007; Patten et al., 2008). After accounting for the effects of prior physical illness, as well as age, tobacco smoking, drinking problems, physical activity, and financial resources, baseline depression was significantly linked to physical illness during the 10-year follow-up. These analyses are conservative in that some prior illnesses may have been consequent to depression, and earlier illness was the most potent predictor of subsequent illness. In these prospective analyses, depressed patients showed a two-thirds higher likelihood of experiencing physical illness during

the follow-up period compared to community controls. Further, after accounting for prior physical illness, as well as for key demographic and health behavior factors at baseline, the association between depression and subsequent physical illness was evident for both less serious and more serious physical illness. The effects for depression on physical illness did not vary as a function of age, gender, health behaviors, or financial resources.

Moreover, consistent with prior literature focusing on specific illnesses (for reviews, see Knol et al., 2006; Rugulies, 2002; Wulsin and Singal, 2003), a prospective link between depression and physical illness was evident for almost half of the medical conditions we examined across a wide spectrum of illness seriousness, and an additional condition, high blood pressure, showed a strong statistical trend. Consistent with previous research on depression and incident heart disease (Rugulies, 2002; Wulsin and Singal, 2003), back pain (Currie and Wang, 2005; Larson et al., 2004), and arthritis (Seavey et al., 2003), we found a prospective link between depression and each of these medical conditions. In addition, our finding of a marginally significant prospective association between depression and high blood pressure is consistent with Meyer et al. (2004), who also reported that major depression was associated with a marginally increased risk for incident hypertension. In contrast to previous research on depression and incident diabetes (for a review, see Knol et al., 2006), we did not find a prospective link between depression and diabetes, possibly reflecting sample or measurement differences across studies.

We also found prospective associations between depression and some conditions that, to our knowledge, have not been studied previously in the context of a prospective link between depression and incident physical illness, including kidney disease, liver disease, and anemia. Bianchi et al. (2005) found depressed mood in more than half of patients with cirrhosis of the liver, however, the authors noted a paucity of research on psychological factors in liver disorders. Two studies examined depression and course of illness in chronic kidney disease (Burton et al., 1986; Hedayati et al., 2004), with both studies reporting associations between depression and mortality among patients with chronic kidney disease, who were followed for 1 to 2 years. Onder et al. (2005) found that depressive symptoms were associated with anemia in a sample of older adults. The authors speculated on mechanisms that might link depression with incident anemia, however, their cross-sectional design was not able to disentangle the direction of relationship between depression and anemia. Anemia also may be secondary to other chronic medical conditions, such as liver and kidney disease.

Several pathways may play a role in the link between depression and physical illness. Suggested mechanisms include biological as well as behavioral pathways. Biological mechanisms may include increased platelet adhesion (Walsh et al., 2002), altered autonomic function (Yeragani et al., 2002), and immune dysregulation (Kiecolt-Glaser and Glaser, 2002). In addition, depression adversely affects a range of health behaviors (Leventhal et al., 2008). For example, depressed individuals consume more alcohol (Holahan et al., 2004), smoke more tobacco (Breslau et al., 2004; Kenney et al., 2006), engage in less physical activity (Whooley et al., 2008), eat less healthily (Krauchi et al., 1990), and show lower levels of medical compliance (Bair et al., 2003; Ciechanowski et al., 2000).

Some limitations should be noted in interpreting these results. Self-report measures are subject to common method variance. The association between depression and physical illness may have been due to depressed individuals perceiving themselves as more ill than they were. This concern is mitigated somewhat by our having asked participants to report only physician-diagnosed conditions, which has been found to have acceptable to high levels of agreement with medical data (Barlow et al., 1998; Farmer et al., 2008; Holahan et al., 1995; Martin et al., 2000). Nevertheless, future research is needed to confirm the present findings using objective criteria to index medical conditions, such as a medical examination, medical records, or corroborating information from collaterals. In addition, the measures of tobacco smoking and physical activity were relatively narrow in scope and were limited to current behaviors at baseline. Also, we did not have information about diet, which would have provided an additional control for health behaviors.

In addition, alternative interpretations of our findings are possible that are consistent with reverse effects between physical illness and depression. Unmeasured medical conditions or physical symptoms below diagnostic threshold at baseline may have both engendered depressive reactions at baseline and been linked over time to eventual medical diagnoses of or co-morbidities with the medical conditions we indexed. Although these alternative interpretations would be more plausible in examining depressive symptoms rather than clinical depressive episodes, it remains possible that medical symptoms could have initiated depressive episodes among vulnerable individuals.

Finally, although the depressed patients were matched demographically with the community controls, they are not representative of all depressed individuals in the community. Because the present sample of depressed patients was entering treatment, our findings generalize more narrowly to depressed individuals receiving treatment for depression. The process of initiating treatment may be related to depression severity, treatment-seeking inclinations or skills, or available resources, such as health insurance. Further, receiving treatment may be associated with the course of depression and consequent occupational, social, and health behaviors.

Our findings broaden the growing awareness of the potential link between depression and physical illness (Stover et al., 2003) to encompass a vulnerability of depressed individuals to physical illness more generally. Among its ten concerns in global public health, the World Health Organization recently included the co-morbidity between depression and chronic physical illness (WHO, 2007). Physical illness places heavy additional burdens on depressed individuals, and depression adds to medical health care utilization across primary, specialty, and emergency medical services (Ford et al., 2004). More broadly, the present findings underscore the interplay between emotional and physical health, and they underscore the potential public health costs of depression (Breslau et al., 2004).

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Conflict of interest

No authors have any actual or potential conflict of interest that could inappropriately influence, or be perceived to influence, this work.

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