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The Role of Medical Comorbidity on Outcomes of Major Depression in Primary Care: The Prospect Study

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Abstract

Objective—Our objective was to describe the influence of specific medical conditions on clinical remission of major depression in a clinical trial evaluating a care management intervention among older primary care patients.

Method—Adults 60 years and older were randomly selected and screened for depression. Primary care practices were randomly assigned to Usual Care or to an intervention consisting of a depression care manager offering algorithm-based care for depression. In all, 324 adults meeting criteria for major depression were included in these analyses. Remission and response for depression was defined by a score on Hamilton Depression Rating Scale <10 and by a decrease from baseline $\geq 50\%$, respectively. Medical comorbidity was ascertained through self-report. Cognitive impairment was defined by a score on the Mini-Mental State Examination (MMSE) <24.

Results—In Usual Care, rates of remission were faster in persons who reported atrial fibrillation (AF) compared to persons who did not report AF, and slower in persons who reported chronic pulmonary disease compared to persons who did not report chronic pulmonary disease; rates of response were faster in persons who reported myocardial infarction (MI) compared to persons who did not report MI, slower for persons who reported any vascular disease compared to persons who did not report any vascular disease, and less stable in persons with MMSE <24 compared to persons with MMSE ≥ 24 . In the Intervention Condition, none of the specific chronic medical conditions were significantly associated with outcomes for major depression.

Conclusions—Because disease-specific findings were observed in persons who received Usual Care but not in persons who received more intensive treatment in the Intervention Condition, our results suggest that the association of medical comorbidity and treatment outcomes for major depression may be determined by the intensity of treatment for depression.

Keywords

Aged; depression; comorbidity; treatment; primary health care

Introduction

Depression is one of the most common problems in primary care settings. Approximately 6-9% of primary care patients suffer from major depression [1]. Although methodologic differences account for variability in estimates, depression occurs in at least 20% of persons undergoing treatment for medical conditions [2-5]. To be specific, investigators have documented the association of depression with the following chronic medical conditions: myocardial infarction (MI) [6-8], congestive heart failure [9,10], coronary artery disease [11], stroke [12], diabetes [13,14], cancer [15], dementia [16], and urinary incontinence [17]. In particular, the strong association between depression and cardiovascular disease has led to the conceptualization of a subtype of depression termed vascular depression [18]. Older patients with depression have also been found to have an increased risk of death after a MI [8,19,20], disability after stroke [21], and disability with chronic obstructive pulmonary disease [22]. Depression accompanying medical illness poses a challenge to clinicians charged with care but also provides an opportunity to study the interplay of treatment for depression with medical illness [23].

Previous studies have suggested an association between chronic medical conditions and treatment outcomes for depression although the evidence has been conflicting. The recovery rate for major depression has been found to be lower for patients with comorbid medical conditions [24] and the presence of physical illness has been associated with greater chronicity of depression [25,26]. One study found that arthritis, circulatory problems, speech disorders, or skin problems were associated with worse outcomes for depression [27]. In addition, the total burden of medical illness and the number of organ systems involved has been associated with poor treatment outcomes for major depression [28]. However, patients with comorbid medical conditions appear to respond to antidepressants as well as patients without comorbid medical conditions [29,30]. For example, medical burden does not interfere with response to fluoxetine in the elderly [31]. Other investigations used the Cumulative Illness Rating Scale for Geriatrics to yield a quantitative measure of overall medical burden and to abstract specific cerebrovascular risk factors scores and found that, with intensive treatment, medical burden and cerebrovascular risk were not related to depression outcomes [32-34]. Whether a treatment intervention can overcome the influence of specific medical illnesses on the course of depression remains unclear. In particular, information is lacking on the relationship of specific medical conditions to the outcomes of depression in older primary care patients in the context of an intervention trial.

The PROSPECT Study (Prevention of Suicide in Primary care Elderly: Collaborative Trial) was a multisite effectiveness trial designed to assess the use of care management on reducing major risk factors for suicide in late life, primarily depression [35-37]. The PROSPECT intervention involved a depression care manager providing algorithm-based care for the elderly. Ethnically diverse patients from community-based primary care practices were carefully screened and sampled to ensure the representativeness of the final sample.

Because a depression care manager providing care in primary care practices is both costly and time intensive, we sought to identify which patients with specific medical illnesses would benefit the most from the intervention. To provide a more detailed analysis of our data, we examined both remission of depression and response to depression treatment as outcomes. Remission, defined as an almost asymptomatic state, is a critical clinical goal in the care of depression. Patients left with residual depressive symptoms have functional impairment, compromised quality of life, and high utilization of health care services [38]. Moreover, remission is a stable clinical state with a lower risk for relapse than improvement of depression that leaves the patient with residual symptoms [39-42]. Remission, therefore, is a more optimal

goal than measures of response of depression, typically defined as 50% reduction of symptoms since baseline, which is the focus of most pharmacological studies.

Our analysis had two goals. The first goal was to identify medical conditions in an intervention trial associated with poor remission and response rates of major depression in elderly primary care patients. Consistent with previous research on specific medical illnesses and treatment outcomes for depression [27], we hypothesized that older persons with specific medical illnesses with ongoing symptoms, e.g. arthritis, often associated with ongoing pain, or heart failure, often associated with ongoing fatigue, would be less likely to achieve remission. We hypothesized that the mechanisms linking specific medical conditions with ongoing symptoms with poor outcomes for depression might be biological, psychological, as well as social. For example, an increase in the number of medications increases the risk of drug-drug interactions and side effects, a higher than expected level of functional disability from the medical condition may lead to diminished life satisfaction, and the requirement of increasing amounts of overall care may stress a social support network. The second goal was to examine whether the intervention of the PROSPECT study modified the impact of medical conditions on the outcomes of depression. Specifically, we hypothesized that the PROSPECT intervention would modify the effects of medical comorbidity seen in usual care, particularly among persons with medical conditions requiring ongoing symptom management.

Methods

The PROSPECT Study

The PROSPECT Study compared a primary care-based intervention with usual care in improving the outcomes of major depression. All study procedures were implemented with written informed consent from the Institutional Review Board of Cornell University, the University of Pittsburgh, and the University of Pennsylvania Schools of Medicine. Details of the study design of the PROSPECT Study are available elsewhere [35-37]. In brief, twenty primary care practices from greater New York City, Philadelphia, and Pittsburgh participated in the study. Practices were paired within each region according to the size of the practice, whether the practice was community-based or academically affiliated, and according to the ethnic distribution of the patient population. Within each pair, practices were randomly assigned to either the Intervention Condition or Usual Care (described below).

A two-stage sampling design was used to recruit patients. First, an age-stratified (60-74 years, over 75 years) random sample of patients with an upcoming appointment was obtained. The sampled patients were sent a letter by mail allowing patients to decline if they did not wish to be contacted. Second, trained lay interviewers telephoned the patients who did not decline. Patients who gave oral consent were screened for depressive symptoms using the Centers for Epidemiologic Studies Depression scale (CES-D) [43]. Screening with the CES-D was offered only to patients who were 60 years or older, able to give informed consent, had a Mini-Mental State Examination (MMSE) [44] ≥ 18 , and were able to communicate in English. Patients with hearing impairment were screened in person at the practice office. All patients were invited into the study with a CES-D score >20 and in addition, a 5% random sample of patients with lower scores were also invited to participate. Furthermore, patients with a CES-D score ≤ 20 and who were not selected randomly were recruited if they responded positively to supplemental questions about prior depressive episodes or treatment. Participants who agreed to be part of the study were scheduled for an in-person interview at the primary care practice site. Participating patients also were administered telephone assessments at 4 and 8 months and an in-person interview at one year.

Intervention Condition

The intervention has been described in detail elsewhere [35]. Briefly, the intervention consisted of trained depression care managers offering guideline concordant recommendations to the primary care physicians and helping patients with adherence to treatment. Patients who refused antidepressants and those who requested or required interpersonal psychotherapy (IPT) were offered IPT by the depression care managers. In the Intervention Condition, the cost of the first line antidepressant, the selective serotonin inhibitor (citalopram), and the IPT was covered for the participants.

Usual Care

In Usual Care, physicians received patients' depression diagnoses. Physicians also received informational materials on geriatric depression and treatment guidelines for depression. However, no specific recommendations were given to physicians regarding individual patients except for psychiatric emergencies.

Depression diagnoses

Trained research assistants (Ph.D., M.A. or experienced B.A. level) assigned depression diagnoses to patients using the Structured Clinical Interview for Axis I DSM-IV Diagnoses (SCID) [45]. Study psychiatrists reviewed all the SCID ratings. Severity of depression was assessed using the 24-item Hamilton Depression Rating Scale (HDRS) [46]. Consistent with other geriatric depression studies [38], remission was defined as a HDRS score lower than 10. For geriatric depression, a HDRS score lower than 10 is often used because older patients often have chronic medical conditions which result in somatic symptoms that are reflected in the HDRS score. In addition to the use of HDRS score less than 10 to define remission, we repeated the analyses using a change in the HDRS scores $\geq 50\%$ as a marker for response to treatment.

Medical comorbidity

Persons were classified as having a medical comorbidity by self-report. The questionnaire used was based on the Charlson Comorbidity Index, supplemented by questions about the common disabling conditions of late life [47]. Participants were asked about myocardial infarction, heart failure, angina, angioplasty or coronary artery bypass surgery, atrial fibrillation, stroke, peripheral vascular disease, high blood pressure, diabetes, cancer, chronic pulmonary disease, peptic ulcer disease, and joint disease. Persons were considered to have any heart disease if they gave a positive response to any of the following: myocardial infarction, heart failure, angina, angioplasty or coronary artery bypass surgery, or atrial fibrillation. Persons were considered to have any vascular disease if they gave a positive response to any of the following: myocardial infarction, heart failure, angina, angioplasty or coronary artery bypass surgery, atrial fibrillation, stroke, peripheral vascular disease, high blood pressure, or diabetes. Cognitive status was assessed with the Mini-Mental State Examination (MMSE) which is a short standardized mental status examination that has been widely employed for clinical and research purposes [44]. The MMSE has been extensively studied, as reviewed by Tombaugh and McIntyre [48] and by Crum and her colleagues [49]. The MMSE assesses orientation to time and place, registration, memory, attention and concentration, praxis, and constructional and language capacity. MMSE scores were analyzed as a dichotomous variable with scores less than 24 representing cognitive impairment. Total medical burden was calculated by adding up the number of medical conditions. The median number of medical conditions in our sample was 4, and persons with 4 or more conditions were considered to have high medical burden.

Analytic strategy

Our data analysis proceeded in two phases corresponding to the two aims of the study. In the first phase, we estimated the remission and response rates for depression in patients with

specific chronic medical conditions as well as in patients with high medical burden. An estimate of association (relative odds) along with a corresponding standard error and a p-value (two-tailed) was produced for individual chronic medical conditions with remission of depression (HDRS <10) and response of depression (change in the HDRS scores $\geq 50\%$) as the outcome at 4, 8, and 12 months according to group assignment. These analyses were based on longitudinal models with random effects for clustering by patient, practice, or practice pairs. For all longitudinal and depression outcomes, clustering by practice and pairs of practice was negligible and did not affect the analysis. All models were adjusted for baseline HDRS score and for the presence or absence of suicidal ideation. We augmented this analysis with additional analyses adjusting for age, gender, and ethnicity. The omnibus test statistic was calculated representing a test of the statistical significance of the time by group interaction [50,51]. In phase two, we were interested not only in whether the intervention was effective in the face of chronic medical illness, but also in whether the intervention modified the relationship between chronic medical conditions and remission of depression. To accomplish this aim, we introduced terms representing the interaction between presence of a chronic medical condition and the intervention condition into separate models for each medical condition. Both the PROC NLMIXED and the GLIMMIX macros in SAS were used to employ 2- and 3-level random effects models, respectively, for binary outcomes. For all our analyses, we set α at 0.05, recognizing that tests of statistical significance are approximations that serve as aids to interpretation and inference. We report actual p-values so that readers can apply their multiple comparisons procedure of choice.

Results

Study sample

The results of screening and enrollment for the PROSPECT study have been described in detail elsewhere [35]. In brief, the study screened 9,072 older persons, and 1,888 persons were invited to participate. Out of the 1,888 persons invited to participate, 1,238 (65.8%) agreed to a baseline interview. Our study sample included 396 persons who met criteria for major depression. Seventy-two people were excluded because they did not complete a four month follow-up visit, leaving a sample size of 324 for this analysis.

Study characteristics

The mean age of our study sample was 69.5 years with a standard deviation of 7.7 years. The age range was 60 to 90 years. Two hundred and forty (74.1%) of the participants were women. The self-identified ethnic groups of the participants consisted of 233 whites (68.8%), 93 African-Americans (28.7%), and 8 American Indians, Hispanics or Asians (2.5%).

Medical comorbidity and clinical remission and response

There were differences in the rates of remission between persons with less than 4 medical conditions versus persons with 4 or more medical conditions (omnibus chi square=10.84; $p=0.013$) with 40% remission at 4 months, 42% at 8 months and 53% at one year versus 23%, 35%, and 45%, respectively. The rates of response did not differ significantly between groups. However, looking at total number of conditions in this way obscures the clinically-relevant relevant differences in outcomes between specific disorders as demonstrated in Table 1.

Medical comorbidity and clinical remission according to group assignment

Corresponding to our first aim, we evaluated the association of specific medical conditions and clinical remission (HDRS <10) according to group assignment using multiple logistic regression. The results for the usual care practices presented in the leftmost columns of Table 2 demonstrate significant omnibus trends for only two chronic medical conditions (atrial

fibrillation and chronic pulmonary disease). Older adults with atrial fibrillation in usual care were significantly more likely to achieve remission at 4 and 8 months than were older adults without atrial fibrillation in usual care. The small number of persons with atrial fibrillation precludes the estimation of a stable relative odds estimate for 12 months in usual care. In models that controlled for age, gender, and ethnicity the association between atrial fibrillation and clinical remission remained significant ($p=.001$). Older adults with chronic pulmonary disease in usual care were less likely to achieve remission at 4 and 8 months but were more likely to achieve remission at 12 months than were older adults without chronic pulmonary disease in usual care. In models controlling for age, gender, ethnicity, and functional status the association between chronic pulmonary disease and clinical remission remained statistically significant ($p=.004$).

The results for remission (HRDS <10) for the intervention practices presented in the middle columns of Table 2 demonstrate that in the intervention practices, none of the chronic medical conditions had a statistically significant influence on the remission rate. In other words, persons with chronic medical conditions were as likely to remit as were persons without chronic medical conditions in the intervention group.

Corresponding to our second aim, we examined each interaction between intervention assignment and specific medical condition. Our results, presented in the rightmost column of Table 2, yielded a statistically significant modification of the probability of remission only for patients with atrial fibrillation.

Medical comorbidity and response according to group assignment

The next set of analyses parallels the previous section; however, the outcome now is change in HDRS scores $\geq 50\%$. The results presented in the leftmost columns of Table 3 demonstrate that a history of myocardial infarction in usual care was significantly associated with a greater occurrence of a change in HDRS $\geq 50\%$ at 4, 8, and 12 months when compared to patients who did not report a history of myocardial infarction in usual care. In the models adjusting for age, gender, and ethnicity, this association remained significant ($p=.02$). In contrast, older adults with any vascular disease in usual care were significantly less likely to achieve a change in HDRS $\geq 50\%$ at 4 months and subsequent interviews than were older adults without vascular disease in usual care. The findings related to persons with vascular disease approached but did not reach statistical significance in models adjusting for age, gender, and ethnicity ($p=.052$). In addition, older adults with a MMSE <24 in usual care were more likely to achieve remission at 4 and 8 months but they were less likely to maintain it at 12 months. The findings related to MMSE score remained significant in the models adjusting for age, gender, and ethnicity ($p=.006$).

The results for change in HDRS $\geq 50\%$ presented in the middle columns of Table 4 demonstrate no statistically significant associations of specific physical illnesses with change in HDRS scores in the intervention condition.

As shown in the rightmost column of Table 4, there were no statistically significant interactions between the presence of specific medical illnesses and the intervention condition in the set of analyses with change in HDRS $\geq 50\%$ as the outcome.

Discussion

Identifying a subset of older persons with specific chronic medical conditions at high risk for poor outcomes of major depression is important in order to enhance the treatment for depression in primary care. The principal finding of this study was that chronic pulmonary disease and vascular disease were associated with low remission and response rates of depression during

the early phases of follow up in older patients receiving usual care, while comorbid cognitive impairment was associated with a less stable remission in usual care. Importantly, no medical illness or cognitive disorder influenced the remission and response rates of depression in patients of primary care practices implementing PROSPECT's intervention. The intervention appears, at least in part, to overcome the effects of medical comorbidities.

Before discussing our findings, the results must first be considered in the context of some potential study limitations. First, we obtained our results only from primary care sites in greater New York City, Philadelphia, and Pittsburgh, whose patients may not be representative of other primary care practices in the United States. However, the participating practices were diverse and consisted of community-based urban and rural practices of varying sizes as well as academically affiliated practices. Second, there is the potential for all the sources of error associated with retrospective interview data including imperfect recall and response bias. Third, selection bias is a potential limitation because, although the larger project was based on a random sample of primary care patients, the data on medical comorbidity and clinical remission of depression consisted of all who were selected for the larger project, agreed to participate, and had complete information. Fourth, although more frequent follow-up would have been desirable, concerns about participant burden and cost led us to select few, yet clinically meaningful, follow-up times. Finally, treatment may have changed frequently both in the intervention and the usual care practices and our analyses do not account for change in treatment.

Nonetheless, despite limitations our results deserve attention because we attempted to evaluate the effect of different chronic medical conditions on outcomes for major depression in primary care. Our results are not wholly consistent with our initial hypotheses. Summarizing our findings relating to our first aim, we observed four distinct patterns for the effect of medical conditions on depression outcomes. Most conditions had no impact on outcomes. Some conditions, such as myocardial infarction and atrial fibrillation in usual care, were associated with improved outcomes. Conversely, vascular disease in usual care was associated with worse outcomes. Chronic pulmonary disease in usual care was associated with delayed remission or response. Finally cognitive impairment in usual care was associated with a less stable response, with outcomes comparable to those for other patients over the short term, but with a worse response over time. By contrast, the depression outcomes for patients in the Intervention Condition did not significantly differ among persons with and without specific medical illnesses, regardless of the outcome criterion.

The reasons for our findings are not entirely clear. The differences in depression outcomes might be due to the different nature of the medical conditions with some presenting as episodic events, e.g. myocardial infarction and atrial fibrillation, and others which have ongoing symptoms, e.g. chronic pulmonary disease. Our findings of lower rates of response seen with vascular disease which approached but did not reach statistical significance in our final models are consistent with the studies by Alexopoulos and colleagues on vascular depression [18]. Overall the findings support the hypothesis that specific medical conditions may influence depression outcomes in Usual Care but the mechanisms have yet to be fully understood. There may be unmeasured biological, psychological, and social mechanisms that are important in explaining the effect of medical conditions with ongoing symptoms versus medical conditions presenting as episodic events on treatment outcomes for depression in Usual Care.

The second aim of our research was to examine whether the assignment to PROSPECT's Intervention Condition or Usual Care modified the relationship between the presence of a chronic medical illness and outcomes for depression. The only significant interaction between the disease effects and treatment assignment was for atrial fibrillation, where the probability of remission appeared to be greatest in usual care participants with the condition. This

observation is difficult to explain, and we cannot exclude the possibility that one interaction out of the large number tested may have appeared to be significant by chance alone. In general, the findings seem to indicate that the effects of medical conditions are apparent in the Usual Care sample, but that they are not significant in the Intervention Condition. For example, a history of MI appeared to increase the rate of response in usual care patients up to that observed in the Intervention Condition. Cardiac disease may represent a “wake-up call” for usual care patients and providers, leading them to focus more carefully on the treatment of depression. In contrast, the delayed response in chronic pulmonary disease may have occurred because chronic pulmonary disease interfered with the management of depression. In addition, the loss of response in individuals with cognitive impairment in Usual Care may have also occurred because cognitive impairment interfered with the management of depression beyond the initial treatment phase. Consistent with these explanations, the lack of significant effects of the illnesses in Intervention patients suggests that the Intervention can, at least in part, overcome the effects of medical comorbidity. Our results are consistent with other studies that found an attenuation of the effect of medical comorbidity on depression outcomes in depression interventions using measures of total medical comorbidity, not specific medical conditions [32-34].

Late life depression often presents in primary care patients with medical comorbidity. We found that certain chronic medical conditions may play a role in depression outcomes among primary care elders but the effect of specific medical comorbidity may be overcome by care management. Our results suggest trained depression care managers combined with algorithm-based care can attenuate the effects of medical comorbidity. Therefore, such interventions can improve the quality of care for late life depression where medical comorbidity is common. Interventions designed to improve depression treatment, to be sustainable and acceptable to physicians and patients, must account for the medical comorbidity that commonly accompanies depression in older persons. Identifying patients with specific chronic medical conditions who will benefit most from special attention may be key to improving outcomes for depression in primary care. The integration of treatment for depression with the treatment for specific medical conditions should be considered.

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Table 1
Clinical remission and response for patients with major depression affected by specific conditions (n=324)

Medical comorbidity	Presence of disease	Remission of depression (HDRS<10). % (n)			Response (>50% change in HDRS). %*		
		4 month	8 month	12 month	4 month	8 month	12 month
Myocardial infarction	present	38 (58)	47 (53)	52 (42)	47	53	57
	absent	31 (258)	38 (237)	49 (217)	30	35	48
Heart failure	present	27 (22)	33 (21)	44 (18)	27	33	44
	absent	33 (302)	40 (278)	50 (249)	33	38	51
Angina	present	23 (95)	33 (82)	43 (76)	32	39	47
	absent	36 (224)	42 (211)	52 (186)	33	38	51
Angioplasty or Bypass surgery	present	34 (47)	44 (43)	44 (36)	45	49	50
	absent	32 (272)	38 (250)	50 (226)	31	36	50
Atrial fibrillation	present	36 (22)	54 (24)	65 (17)	50	58	53
	absent	33 (289)	38 (263)	48 (240)	32	37	50
Any heart disease	present	27 (138)	36 (121)	49 (111)	32	36	50
	absent	36 (179)	41 (170)	50 (149)	34	39	50
Stroke	present	29 (82)	35 (74)	48 (62)	32	39	55
	absent	33 (237)	41 (219)	50 (200)	33	38	49
Peripheral vascular disease	present	26 (108)	42 (96)	48 (84)	32	37	50
	absent	36 (211)	38 (197)	51 (178)	34	40	50
High Blood Pressure	present	32 (220)	39 (198)	49 (180)	33	40	51
	absent	33 (98)	39 (94)	51 (82)	33	35	48

Medical comorbidity	Presence of disease	Remission of depression (HDRS<10), % (n)			Response (>50% change in HDRS), %*		
		4 month	8 month	12 month	4 month	8 month	12 month
Diabetes	present	22 (72)	33 (67)	43 (56)	32	39	39
	absent	35 (246)	41 (225)	52 (205)	33	38	53
Any vascular disease	present	31 (281)	39 (255)	48 (225)	31	38	49
	absent	46 (37)	41 (37)	58 (36)	46	38	56
Cancer	present	24 (42)	38 (40)	46 (37)	33	45	57
	absent	33 (275)	39 (251)	50 (223)	33	37	49
Chronic pulmonary disease	present	24 (100)	40 (85)	55 (73)	31	40	58
	absent	36 (219)	39 (208)	48 (189)	34	38	47
Peptic ulcer disease	present	17 (35)	28 (32)	53 (30)	20	25	63
	absent	34 (282)	41 (258)	49 (230)	34	40	48
Joint disease	present	28 (192)	38 (178)	48 (154)	29	38	50
	absent	39 (121)	41 (111)	52 (104)	40	40	50
MMSE < 24	present	26 (31)	31 (26)	44 (25)	35	38	28
	absent	33 (293)	40 (273)	50 (242)	33	38	53

Note: Data gathered from the PROSPECT study. HDRS = Hamilton Depression Rating Scale; MMSE = Mini-Mental State Examination.

* N is the same as for remission

Table 2
Relative odds for remission (HDRS < 10) of major depression for selected medical conditions according to group assignment

	Group Assignment							
	Usual Care		Intervention Condition					
	χ^2 (3df), p-value	RO 4 months	RO 8 months	RO 12 months	χ^2 (3df), p-value	RO 4 months	RO 8 months	RO 12 months
Medical condition								Interaction χ^2 , p-value
Myocardial infarction	3.73, .29	.387	4.95	3.33	.34, .95	.99	1.26	.74
Heart failure	3.59, .31	.68	.29	10.76	.98, .81	.38	1.02	.41
Angina	3.41, .33	.34	.23	.66	7.56, .06	.17	.83	.60
Angioplasty or Bypass surgery	1.91, .59	2.28	3.57	1.10	.44, .93	.59	.94	.69
Atrial fibrillation	14.59, .002*	1.45	6.94	**	2.15, .54	1.17	2.86	.32
Any heart disease	2.53, .47	.57	.67	1.97	5.30, .15	.24	.71	.78
Stroke	.57, .90	.73	.52	.95	1.18, .76	.61	.92	1.38
Peripheral vascular disease	4.16, .24	.18	.82	.61	4.68, .20	.61	2.62	1.46
High blood pressure	.62, .89	.54	.80	.93	.22, .97	1.08	1.26	1.36
Diabetes	6.78, .079	.09	.47	.16	4.91, .18	.30	.61	1.73
Any vascular disease	6.42, .09	.09	.85	.30	1.50, .68	.40	1.43	1.15
Cancer	1.61, .66	.26	.60	.52	.06, .99	1.13	1.27	1.13
Chronic pulmonary disease	12.20, .007*	.27	.77	9.04	4.49, .21	.33	1.45	1.13
Peptic ulcer disease	3.41, .33	.23	.37	1.85	2.82, .42	.20	.30	1.88
Joint disease	4.28, .23	.30	.40	1.31	3.90, .27	.35	1.03	.44
MMSE <24	1.97, .58	1.74	.61	.29	2.13, .55	.21	.38	.74

Notes: Data gathered from the PROSPECT study. RO = Relative odds; HRDS = Hamilton Depression Rating Scale; MMSE = Mini-Mental State Examination. χ^2 , 3df represents an omnibus test. Relative odds estimates are adjusted for baseline HDRS and suicidal ideation.

* P<0.05.

** The number of cases of atrial fibrillation was too small to yield a stable RO estimate.

Table 3
Relative odds for response (Change in HRDS ≥50%) of major depression for selected medical conditions according to group assignment

	Group Assignment							
	Usual Care				Intervention Condition			
Medical condition	χ^2 (3df), P-value	RO 4 months	RO 8 months	RO 12 months	χ^2 (3df), P-value	RO 4 months	RO 8 months	RO 12 months
Myocardial infarction	1005, .016*	8.10	5.65	2.73	2.17, .54	1.73	2.16	.88
Heart failure	.26, .97	.80	.70	1.10	.29, .96	.68	.61	.74
Angina	1.15, .77	1.43	1.29	.62	1.21, .95	.56	.84	1.05
Angioplasty or Bypass surgery	6.03, .11	6.25	3.60	2.23	1.00, .80	1.46	1.31	.67
Atrial fibrillation	6.82, .078	1.25	16.97	1.83	4.41, .22	7.64	1.88	1.84
Any heart disease	.20, .98	1.34	1.23	1.16	1.31, .73	.63	.61	1.00
Stroke	0.0, 1.00	.62	.78	.86	3.51, .32	.98	1.38	2.77
Peripheral vascular disease	5.49, .14	.20	.86	.74	1.42, .70	.99	1.79	1.31
High blood pressure	.33, .95	.74	1.38	1.05	1.69, .64	1.27	1.54	2.03
Diabetes	7.69, .053	.53	1.42	.16	.35, .95	.97	.79	.74
Any vascular disease	8.72, .03*	.12	.73	.21	.09, .99	.60	1.56	2.04
Cancer	1.42, .70	.54	1.21	1.45	2.96, .40	3.25	2.61	2.85
Chronic pulmonary disease	2.84, .42	.70	1.20	2.17	2.07, .56	.96	1.09	2.34
Peptic ulcer disease	5.81, .12	.62	.54	3.75	2.85, .42	.38	.41	2.39
Joint disease	2.15, .54	.35	.73	.97	4.18, .24	.41	.90	1.11
MMSE <24	13.88, .003*	1.59	3.22	.05	1.35, .72	.73	.33	.36

Notes: Data gathered from the PROSPECT study. RO = Relative odds; HRDS = Hamilton Depression Rating Scale; MMSE = Mini-Mental State Examination. χ^2 , 3df represents an omnibus test. Relative odds estimates are adjusted for baseline HDRS and suicidal ideation.
* P<0.05.

Table 4
Odds ratios for response (Change in HRDS > 50%) of major depression for selected medical conditions according to group assignment

	Group Assignment							
	Usual Care				Intervention Condition			
Medical condition	χ^2 (3df), P-value	OR 4 months	OR 8 months	OR 12 months	χ^2 (3df), P-value	OR 4 months	OR 8 months	OR 12 months
Myocardial infarction	1005, .016*	8.10	5.65	2.73	2.17, .54	1.73	2.16	.88
Heart failure	.26, .97	.80	.70	1.10	.29, .96	.68	.61	.74
Angina	1.15, .77	1.43	1.29	.62	1.21, .95	.56	.84	1.05
Angioplasty or Bypass surgery	6.03, .11	6.25	3.60	2.23	1.00, .80	1.46	1.31	.67
Atrial fibrillation	6.82, .078	1.25	16.97	1.83	4.41, .22	7.64	1.88	1.84
Any heart disease	.20, .98	1.34	1.23	1.16	1.31, .73	.63	.61	1.00
Stroke	0.0, 1.00	.62	.78	.86	3.51, .32	.98	1.38	2.77
Peripheral vascular disease	5.49, .14	.20	.86	.74	1.42, .70	.99	1.79	1.31
Any vascular disease	.82, .84	.58	.83	.87	.26, .97	1.10	.85	1.13
High blood pressure	.33, .95	.74	1.38	1.05	1.69, .64	1.27	1.54	2.03
Diabetes	7.69, .053	.53	1.42	.16	.35, .95	.97	.79	.74
Cancer	1.42, .70	.54	1.21	1.45	2.96, .40	3.25	2.61	2.85
Chronic pulmonary disease	2.84, .42	.70	1.20	2.17	2.07, .56	.96	1.09	2.34
Peptic ulcer disease	5.81, .12	.62	.54	3.75	2.85, .42	.38	.41	2.39
Joint disease	2.15, .54	.35	.73	.97	4.18, .24	.41	.90	1.11
MMSE <24	13.88, .003*	1.59	3.22	.05	1.35, .72	.73	.33	.36

Notes: Data gathered from the PROSPECT study. OR = Odds ratio; HRDS = Hamilton Depression Rating Scale; MMSE = Mini-Mental State Examination. χ^2 , 3df represents an omnibus test. Odds ratios are adjusted for baseline HDRS and suicidal ideation.
* P<0.05.