Antidepressant therapy in primary care:
Does patient preference affect response?

By

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Context Current research and practice guidelines support the use of both psychotherapy and pharmacotherapy for the treatment of depression in primary care. Identifying predictors of response to therapy can assist patients and providers in choosing the most effective treatment for individual patients.
Objective To assess the effect of patient treatment preference on therapeutic outcome in a trial of antidepressant therapy for patients with depressive symptoms.
Design Secondary analysis of a randomized, controlled trial of 3 selective serotonin reputake inhibitors (SSRIs) in primary care.
Setting & Participants A total of 573 patients with symptoms warranting antidepressant therapy in 37 primary care practices organized in 2 U.S. primary care research networks.
Intervention Participants were queried at baseline about the acceptability of antidepressants, counseling, and waiting as treatments for depression before being randomized to one of three SSRIs.
Outcome Measures The two primary outcomes were 1) depressive symptoms, measured by the Symptoms Checklist (SCL-20), and 2) functional status, measured by the Medical Outcomes Study 12-Item Short Form Health Survey Mental Component Summary Score (MCS-12). Outcomes were assessed by telephone interview at 1, 3, 6, and 9 months after initiation of antidepressant therapy.
Results Patients were categorized as having a strong antidepressant preference (23%), mild antidepressant preference (48%), counseling preference (12%), or a preference for waiting (17%). Logistic regression revealed that white race, longer chronicity of symptoms, and a past history of depression treatment were significantly associated with a strong antidepressant preference versus other groups. Longitudinal models demonstrated significant time by preference group interactions for both SCL-20 ($p < 0.001$) and MCS-12 ($p < 0.001$) scores, adjusting for baseline covariates of age, gender, race/ethnicity, anxiety, chronicity of symptoms, past history of depression treatment, and medical comorbidity.
Conclusions Patients who believe antidepressants are a definitely acceptable treatment for depression respond more rapidly to SSRI therapy than other patients. Patient treatment preference is a significant predictor of the rate of response to pharmacotherapy for depression.

Introduction

Patient-centered care is a clinical approach characterized by medical decision-making that is responsive to the knowledge, attitudes, and beliefs of individual patients.[1] In this sense, patient-centered care reflects a professional evolution away from traditional approaches that focus on disease specifics and physician authority. The value of the patient-centered approach has been validated both by surveys that indicate that patients want such a focus in primary care appointments[2] and by research in multiple medical specialities demonstrating that this approach to improving communication produces better health outcomes.[3] Addressing patient preferences for treatment is an important component of the patient-centered approach.

Both depression-specific psychotherapy and antidepressants produce similar clinical benefit in patients treated for depressive disorders.[4,5,6] Because of their equal efficacy, the 1998 Agency for Health Care Policy and Research (AHCPR) practice guidelines for the treatment of major depression in primary care conclude that either treatment is acceptable and that, because predictors of response to either therapy are not well understood, patients' preferences should be taken into account in making decisions regarding therapy.[7] Despite these specific guidelines many primary care patients do not receive adequate therapy for depression,[8] and it is unclear to what extent patient preferences are elicited and incorporated into treatment plans.

Surveys of both depressed and general primary care patients indicate that a majority of patients want active treatment for depression, and that a majority of those preferring active treatment prefer counseling to antidepressants.[9,10,11] Cross-sectional studies have correlated patient treatment preferences with a host of medical and

demographic variables, including gender, race/ethnicity, knowledge about treatment, past history of treatment, and income.[10] Despite the clear evidence that patients prefer counseling for the treatment of depression, few patients in primary care receive psychotherapy and little research has investigated the effect that preferences have on treatment outcomes. Two partially randomized patient preference trials conducted in the United Kingdom have assessed the effect of preferences on outcome for both antidepressants and counseling.[12,13] The studies employed a design in which patients were recruited and randomized to alternative treatments; those who refused randomization but agreed to participate were allowed to choose between alternative treatments, producing four arms: two randomized treatment arms and two preference arms. Comparing those who chose antidepressants to those randomized to antidepressants, no effect on outcome was documented for preference, but one study did find improved outcomes for those preferring counseling compared to those randomized to counseling.

The equivalence of antidepressants and psychotherapy in the treatment of depression underscores the importance of defining predictors of therapeutic response in order to realize safe, effective, and cost-effective care. Among the confirmed predictors for persistence of symptoms and unresponsiveness to therapy are initial severity of depression,[14] neuroticism,[14] chronicity of symptoms,[15] and comorbid panic disorder.[16] Providing patients with treatments that are consonant with their individual values may offer an opportunity to improve outcomes. To further assess the relationship between treatment preference and therapeutic outcomes, we investigated whether patient preferences for treatment affected response to antidepressant therapy in a randomized trial

of selective-serotonin reuptake inhibitors (SSRIs) in primary care. We hypothesized that patients who preferred antidepressant therapy would have a greater response to medical therapy than other patients.

METHODS

Enrollment & Design

A Randomized Trial Investigating SSRI Treatment (ARTIST) was designed to compare the effectiveness of 3 SSRIs in a primary care setting; full details of its methodology have been published elsewhere.[17] Briefly, patients were enrolled over an eight-month period in 1999 in 2 primary care research networks. Eligible patients were aged at least 18 years, received their primary care from a participating provider, and were judged by their provider to have a depressive disorder that merited antidepressant therapy. Exclusion criteria included severe cognitive impairment, terminal illness, actively suicidal, recent or current SSRI use, current non-SSRI antidepressant use, and pregnancy, breastfeeding, or planning pregnancy. The ARTIST study was approved by the relevant institutional review boards; our substudy was approved by the institutional review boards of Duke University and the University of North Carolina School of Public Health.

Clinic personnel obtained informed consent after the primary-care physician (PCP) deemed antidepressant therapy warranted due to clinical suspicion of a depressive disorder. Using a telephone procedure, patients were randomized by balanced blocks to one of three treatment regimens: 20 mg of paroxetine, 20 mg of fluoxetine hydrochloride, or 50 mg of sertraline. Neither patients nor PCPs were blinded to treatment, and the PCP could adjust the dose or change antidepressant based on clinical response. To defray the costs of therapy, enrolled patients were provided with a pharmacy benefits card that covered the cost of SSRI and non-SSRI antidepressants that the PCP prescribed during the 9 month trial. Outcomes were assessed with telephone interviews, with all information, save for suicidal ideation, concealed from PCPs. Study participants were

financially compensated on a per-interview basis, with a maximum total reimbursement of $150.

Baseline Assessment

Patient preferences were assessed with the three questions: "When you feel sad, how acceptable is it for you to… 1) wait and get over it naturally, 2) use anti-depressant drugs, and 3) seek one-on-one counseling from a mental health professional?" Possible patient responses were "Definitely acceptable," "Probably acceptable," "Probably not acceptable," "Definitely not acceptable," or "Don't know." Using responses to the baseline treatment preference questions, patients were assigned to one of four mutually exclusive preference groups: 1) those responding that antidepressants were definitely acceptable (strong antidepressant preference), 2) those responding that antidepressants were probably acceptable (mild antidepressant preference), 3) those who felt that antidepressants were either probably not or definitely not acceptable but responded that counseling was definitely or probably acceptable (counseling preference), or 4) those who felt that neither antidepressants nor counseling was definitely or probably acceptable (waiting preference). For group assignment, "Don't know" was treated as a response of unacceptable.

We measured patient characteristics that affect response to antidepressant therapy, including severity and chronicity of depression, prior history of depression treatment, coexisting anxiety disorder, and comorbid medical conditions.[14-16] Chronicity of symptoms was approximated by grouping diagnoses as determined by patient responses to questions assessing the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV)* depressive disorder diagnostic criteria. Patients were grouped into

either 1) double depression or dysthymia, 2) major depression or bipolar disorder, 3) minor depression, or 4) no depressive diagnosis. Because some patients had multiple diagnoses, the diagnosis of double depression or dysthymia took prominence. Patients were queried for any past treatment for depression, and anxiety was assessed with a three-question anxiety disorder screen adapted from the Primary Care Evaluation of Mental Disorders (PRIME-MD), with questions assessing generalized anxiety and panic attacks.[18] Although specific report of medical comorbidities was unavailable, self-report of baseline medication use was used to calculate each patient's Chronic Disease Score (CDS), a validated proxy for comorbid conditions that is highly correlated with individual health care costs and mortality.[19]

Outcome Measures

There were two outcomes for assessing response to therapy. Depressive symptoms were assessed with the Symptoms Checklist 20 (SCL-20), a subset of the Hopkins Symptom Checklist and Brief Symptom Inventory that has been validated as a measure of depression severity in several randomized trials of depression therapy.[20,21,22] Lower scores on the SCL-20 indicate fewer depressive symptoms, and a mean (SD) depressive symptom score of 1.14 (0.28) for the U.S. population has been reported.[23] Functional status was measured by the Medical Outcomes Survey 12-Item Short-Form Health Survey Mental Component Summary (MCS-12), which incorporates four of the SF-12 subscales into a composite measure of mental health and is highly correlated with the more extensive SF-36 MCS.[24] Higher MCS-12 scores indicate better functional status, and normative testing has established the mean (SD) MCS-12 score for the U.S.

population as 50.04 (9.6), with a range of 10-70.[24] All outcomes were assessed at 1, 3, 6, and 9 months after beginning antidepressant therapy.

Statistical Analysis

Descriptive statistics, including means, standard deviations, medians and ranges, were calculated for all baseline variables. To examine baseline differences between groups, means of continuous variables and percentages of categorical variables were compared with one-way analysis of variance (ANOVA) (or Kruskal-Wallis analysis of variance where appropriate) and Pearson's chi-square test, respectively.[25]

Using the baseline data, a multinomial logistic regression model was used to determine independent predictors of preference group, in order to identify potential covariates for the main statistical model.[25] Categorical variables for chronicity and race were entered into the model as indicator variables. The model was refined with reverse stepwise elimination of variables, with each successive model compared to the saturated model with the likelihood ratio test.[25] A P-value < 0.05 was considered to be significant for all analyses.

To describe the longitudinal outcome variables, mean changes in scores both from baseline and from previous timepoint were calculated for each preference group. Mean scores of both outcomes – SCL-20 and MCS-12 – were compared between preference groups at each timepoint using oneway ANOVA.[25] In order to utilize the advantage of multiple observations on single individuals, repeated-measures analysis of covariance (ANCOVA) models for both outcomes were used to better analyze the data longitudinally.[25] The models incorporated both the main effects of interest – preference group and preference group by month – but also the baseline covariates for age, gender,

race/ethnicity, baseline anxiety score, baseline SCL-20 or MCS-12 score, chronicity of symptoms by depressive diagnosis, past history of depression treatment, and the Chronic Disease Score.

To better incorporate both fixed and random effects, the data were reanalyzed in collaboration with statisticians at the Durham, NC VA Medical Center using linear mixed-effects models to compare the changes in the main outcomes over time between preference groups.[i] The mixed effects model incorporates both the fixed effects of treatment and covariates and the random effects of individual variability in outcome.[26] Main fixed effects were preference group and both linear and quadratic month by group interactions. Random effects were included for patient and physician. Initial models for both outcomes incorporated only the preference groups and their interaction with both linear and quadratic time variables. Secondary models for both outcomes included not only the main exposure-outcome axis, but also the covariates representing age, gender, race/ethnicity, baseline anxiety score, chronicity of symptoms by depressive diagnosis, past history of depression treatment, randomized SSRI, and the Chronic Disease Score. Using these models, predicted values of the outcome scores over time were calculated. All analyses were performed using STATA v7.0 (STATA Corp., College Station, TX), except the mixed-effects model, which was fit using PROC MIXED in SAS v8.0 (SAS Institute, Cary, NC).

[i] Thanks to Maren Olsen, Ph.D. and Di Liu of the Biostatistics unit of the Institute for Clinical and Epidemiologic Research at the VA Medical Center in Durham, NC, for developing the mixed-effects models.

RESULTS

Baseline Characteristics

Participant flow through ARTIST is shown in Figure 1. Of the 688 patients invited to participate, 601 were randomized to one of three SSRI treatments and 573 completed the baseline telephone assessment. Follow-up interviews were successfully completed in 94% of patients at 1 month, 87% at 3 months, 84% at 6 months, and 79% at 9 months.

Waiting as a treatment for depression was definitely or probably acceptable to 83% of participants, while antidepressants were acceptable to 71% and counseling to 66% (Table 1). The strong antidepressant preference group comprised the 131 patients who responded that antidepressants were definitely acceptable, and the 276 patients who responded that antidepressants were probably acceptable composed the mild antidepressant preference group. Of the remaining patients, 68 found counseling to be definitely or probably acceptable and constitute the counseling preference group, and the remaining 98 patients found neither antidepressants nor counseling acceptable and were assigned to the waiting preference group.

Characteristics of the 573 patients completing the baseline interview are shown in Table 2 by assigned preference group. Overall, the mean age of study participants was 46, and 79% were women; the study population was 84% white and 13% black. As assessed by the PRIME-MD, 73% of participants had major depression, 48% had dysthymia, 42% had double depression, and 8% had minor depression. Baseline scores on the main depression outcome scales described a study population with moderately

severe depression with mean (SD) scores of 1.66 (0.7) on the SCL-20 and 32.6 (11.5) on the MCS-12.

Significant differences between preference groups were observed for age, race, depressive disorder diagnosis, and past history of depression treatment. While 9.9% of the strong antidepressant preference group had no depressive diagnosis by the PRIME-MD, 25.5% of the waiting preference group had no diagnosis. By preference group, mean (SD) baseline SCL-20 scores ranged from 1.43 (0.82) for the waiting preference group to 1.86 (0.76) for the strong antidepressant preference group, with the baseline differences in SCL-20 scores by exposure group significant ($P = 0.0001$) (Table 3). Post-hoc pairwise comparisons between preference groups using the student's t-test revealed that the group with a strong antidepressant preference was significantly different from all other groups. Mean (SD) baseline MCS-12 scores ranged from 36.7 (13.0) for the waiting preference group to 28.3 (10.6) for the strong antidepressant preference group, with baseline scores again significantly different between exposure groups ($P < 0.0001$) (Table 4). The mean MCS-12 score for the group with a strong antidepressant preference was significantly different from all three other groups.

Of demographic variables and potential covariates, race ($P = 0.032$), chronicity of symptoms ($P = 0.044$), and past history of depression treatment ($P < 0.001$) were independently associated with preference group. Patients who were white, had more severe or chronic depressive symptoms, or had been treated for depression previously were more likely to have a strong antidepressant preference than to prefer counseling or waiting. Age, gender, experiencing recent panic attacks, and the Chronic Disease Score were not significantly associated with preference group.

Response to Therapy

Patients in all preference groups demonstrated substantial improvement as measured by SCL-20 and MCS-12 scores during the study. The overall mean SCL-20 score improved from 1.66 to 0.78; the overall mean MCS-12 score increased from 32.59 to 48.75. Change in both scores was greatest in the first month after treatment initiation, and the rate of improvement in scores decreased during subsequent intervals. The original ARTIST results demonstrated that all three SSRIs produced equivalent outcomes in this group of patients.[17]

Tables 3 and 4 summarize the change over time in SCL-20 and MCS-12 scores, respectively, by treatment preference group. Figures 2 and 3 illustrate these score changes graphically. Although scores on both outcomes are significantly different at baseline between preference groups for both SCL-20 ($P = 0.0001$) and MCS-12 ($P < 0.0001$), this difference was insignificant in subsequent measures.

Patients with a strong antidepressant preference demonstrated greater improvement in scores than other groups (Figures 4 and 5). While SCL-20 scores decreased by a mean of 1.10 by 9 months in the strong antidepressant preference group, mean decreases in the other three groups ranged from 0.75 to 0.87 (Table 5). Similarly, mean MCS-12 scores improved by 21.1 at 9 months among those with a strong antidepressant preference, while mean improvements in other groups ranged from 11.9 to 15.3 (Table 6).

Longitudinal analyses revealed that mean SCL-20 and MCS-12 scores for the strong antidepressant preference group improved faster than scores for the other groups. The ANCOVA models documented significant group by time interactions for both SCL-

20 ($P = 0.0001$) and MCS-12 ($P < 0.0001$) models. The mixed-effects model for the SCL-20 indicated significant interactions for both group by time ($P = 0.0005$) and group by time^2 ($P = 0.0368$). The mixed-effects model for the MCS-12 supported a significant interaction only for group by time ($P = 0.0002$), with a nonsignificant interaction for group by time^2 ($P = 0.0660$). For the mixed-effects models, the strong antidepressant preference group was the referent category for all tests. Predicted scores for both SCL-20 and MCS-12 over time for the preference groups based on the mixed-effects models are presented in Figures 6 & 7.

DISCUSSION

In this study we demonstrate that primary care patients with clinical depression meriting antidepressant therapy who report that antidepressants are definitely acceptable respond more quickly to antidepressant therapy than do those who prefer counseling or no treatment at all. Response to therapy was assessed with instruments measuring both depressive symptom severity and functional status. Although patients in all preference groups experienced substantial improvements on these measures during the study, baseline patient preferences significantly affected the rate of response. This effect was adjusted for the confounding influences of patient demographics and medical histories, and was detected with sound longitudinal statistical analyses.

The ARTIST study was designed to simulate typical primary care treatment, allowing a great deal of latitude in treatment options and disease management. Because of the absence of artificial study requirements other than randomization to an SSRI, we believe that the study accurately reflects therapeutic conditions and patient response in primary care settings. We investigated patient preferences and treatment outcome in a study in which all patients were recruited with the knowledge that they would receive antidepressant therapy. This selection method had the potential to minimize differences in outcomes between preference groups by eliminating those patients who were more opposed to pharmacotherapy. Because of this, it is possible that the effect of preference on treatment outcome is larger than we report.

Patient Preferences

The patient preferences elicited with our assessment are similar to those of other studies. Interviewing 368 primary care patients who met the Composite International

Diagnostic Interview criteria for a major depressive episode, Cooper-Patrick *et al.* found that while 86% of patients considered individual counseling to be an acceptable treatment, only 70% considered antidepressants acceptable and 69% responded that waiting and getting over it naturally was acceptable.[27] Dwight-Johnson *et al.* surveyed depressed primary care patients about treatment preferences; over 80% preferred active treatment to no treatment, and a majority of those preferring active treatment would choose counseling over antidepressants.[10] Churchill *et al.* found that 51% of consecutive primary care patients preferred counseling and 15% favored pharmacotherapy.[9] Our findings were notable for a greater acceptability of waiting than either active treatment, and a greater acceptability of antidepressants than counseling. We selected for patients who were amenable to antidepressant therapy and we included patients with no depressive diagnosis (approximately 12% of patients), resulting in a different patient population with slightly different preferences.

The difference in preferences between studies highlights the variability in methods used to elicit treatment preferences. Cooper-Patrick *et al.* used an instrument similar to ours, which relied on basic questions about single treatments with a range of answers regarding acceptability. In contrast, Churchill *et al.* presented patients with four treatment options which they were instructed to rank in order of preference; Dwight-Johnson *et al.* employed a single question about five treatments which described the cost, duration, and probability of success of each treatment, and which required patients to choose the one treatment they preferred. Forcing patients to choose the most preferred method prevents overlap of acceptable treatments, and incorporating specific treatment information reduces potential knowledge deficits. However, without a validated and

consistent instrument for eliciting patient preferences, drawing general conclusions from research in this field will be difficult.

Despite the heterogeneity of preference assessment instruments, our preference groups reflect previous patient profiles. We found that white patients, more severely and chronically depressed patients, and those with a history of depression treatment were more likely to have a strong preference for antidepressants. Dwight-Johnson *et al.* found that antidepressant preference was more likely among patient who were white, female, had more knowledge of treatments, had a history of treatment, and had higher incomes. Similarly, a more limited assessment by Cooper-Patrick *et al.* found that African Americans were more likely to find medications unacceptable than white patients.[27] Our study rested heavily on extracting a convincing measure of preference as our main exposure variable, and the fact that our categorization scheme agrees with previous research validates its application.

Treatment Outcomes

We document an association between patient preference and response to antidepressant therapy. Previous studies of patient preference and treatment outcome in depression have produced mixed results. The United Kingdom Counseling versus Antidepressants in Primary Care Study Group conducted a partially randomized preference trial that allowed patients to refuse randomization to either counseling or antidepressants and choose between the treatments. Although patient preference for either antidepressants or counseling conferred no improved outcome at 8 weeks[28], at 12 months the patients choosing counseling had slightly better outcomes than those randomized to counseling.[12] A second trial from the UK with randomized and patient

preference arms that evaluated the effectiveness of counseling, cognitive-behavior therapy, and usual care in depressed primary care patients found no significant differences in depression outcome measures between patients who chose psychological treatments and those who were randomized to them.[13] Rost *et al.* found that the improvement in depression severity attributable to a quality of care enhancement program was potentiated in patients who found antidepressants to be acceptable.[29] Although this suggests that preference plays some role in treatment response, our study is the first that we know of to directly demonstrate improved outcomes with antidepressant therapy for patients who prefer antidepressants.

Our study differs from the preference trials in that all patients were recruited for and assigned to antidepressant therapy regardless of preference, patient preferences were elicited with a more indirect method of assessment, and our study was conducted in the United States, where attitudes towards and knowledge of depression treatment may vary from those in the U.K. Our results suggest the need for more research in the United States exploring depression treatment preferences and their effect on therapeutic outcomes.

A more immediate concern is the clinical significance of the differential response we document. The overall changes in scores from baseline represent clinically important improvements, as this patient population achieved scores after 9 months of therapy that are consistent with population norms. The clinical importance of the differential improvement between preference groups is more difficult to judge. Although patients with a strong preference for antidepressants have greater improvement in scores and respond more rapidly to antidepressants, mean scores for all four preference groups were

similar at 9 months, indicating that a comparable level of depressive symptom severity and functional status was achieved with pharmacotherapy. This suggests that prescribing antidepressants – regardless of patient treatment preference – produces depressive symptom severity and functional status after 9 months of therapy comparable to population norms. Because we document increased rates of improvement with strong preference for antidepressants, however, our study implies that preference affects the amount of time needed to improve clinically significant improvements in symptoms and functional status.

Limitations

Our study has several limitations. First, by assigning all patients to antidepressant therapy regardless of patient preference, our study differs from existing research on the effect of treatment preference on treatment outcome in that patients were not necessarily treated with their preferred therapy; regardless of preference, all patients received antidepressant therapy. Although this is less ideal than other study designs, it may more accurately reflect the reality of depression treatment in the United States, where preferences are often unaddressed and physicians are increasingly utilizing pharmacotherapy at the expense of psychological treatment.[30]

Second, our treatment preference groups were defined indirectly, by abstracting them from responses to questions regarding the acceptability of treatment rather than treatment preference. However, the preference groups we developed reflect previous research that has demonstrated differences in preferences associated with race/ethnicity, chronicity of symptoms, severity of symptoms, and past history of treatment.[10]

Third, because of the nature of our study, baseline characteristics between patients in the four preference groups were different, notably with respect to chronicity of symptoms (as approximated by the depressive disorder diagnosis) and severity of symptoms (as measured by both the SCL-20 and the MCS-12). Because of the confirmed impact of chronicity and severity of depression on treatment outcome,[14,15] these differences had the potential to confound the relationship under investigation between preference and outcome. Because of this, our longitudinal models incorporated the chronicity of symptoms as a covariate and accounted for the severity of symptoms at baseline. The possibility still exists, however, that an unmeasured and maldistributed factor produced the differences between preference groups that we document.

Implications

Our patient preference groups were designed with an eye towards clinical relevance. While more narrowly-defined groups may have provided sharper contrasts between groups and more distinct patient profiles, we chose a simplified categorization scheme which is more amenable to rapid clinical assessment. Our preference groups can be reproduced with a two-step clinical evaluation: 1) assessing the degree of antidepressant acceptability, and 2) assessing the degree of counseling acceptability among those who find antidepressants unacceptable. Although this may not produce the most precise representation of treatment preferences, its association with treatment response validates its utility as a clinical tool.

While assessing preferences in clinical settings may be easy, effectively treating patients who are less likely to respond to antidepressants is more difficult. Although the AHCPR guidelines recommend both antidepressants and counseling with equal vigor,

this recommendation is relevant only when a proven counseling program is accessible. While primary care physicians have relatively uniform access to antidepressant medication, access to effective counseling programs in the United States is more restricted. With a finite number of counselors, few counseling programs proven to be effective, and differential insurance coverage for psychotherapy compared to medical therapy, barriers to receiving counseling for depression are numerous. We investigated only the effect of preference on antidepressant therapy response, but we may presume that patients who prefer counseling respond more quickly to counseling than other patients. Accommodating those patients and providing the most effective and efficient treatment will be difficult without changes in the current mental health system to make effective counseling programs more accessible.

Our study documents an association between a strong preference for antidepressants and improved treatment outcome; we are unable to confirm a causal relationship between this preference and improved outcome. If we infer a causal link between the two, we may surmise that improving patient perceptions of antidepressants and thus making them more preferable is a potential means to improve treatment outcomes. Patients voice a variety of concerns about antidepressants, mainly regarding their side effects, addiction potential, and the necessary length of treatment.[31] Addressing these concerns about pharmacotherapy may make them more acceptable to patients and cause them to respond more quickly than if they were less accepting of antidepressants. Such patient education could be done on an individual level at the outset of therapy or through wider, population-level information campaigns.

Do these results advocate allowing patient preferences to guide depression treatment? The difficulty in designing treatment plans for patients with depressive disorders lies in predicting which treatment will be effective for an individual patient. Our results confirm that a strong preference for antidepressants is a significant predictor of improved response to antidepressant therapy, suggesting it is best to accommodate these patients with pharmacotherapy. How best to accommodate patients with other preferences and ensure the provision of the most effective and efficient care should be the focus of further efforts to apply the principles of patient-centered care to improve depression outcomes in primary care.

Figure 1. Study Enrollment and Follow-up by Preference Group

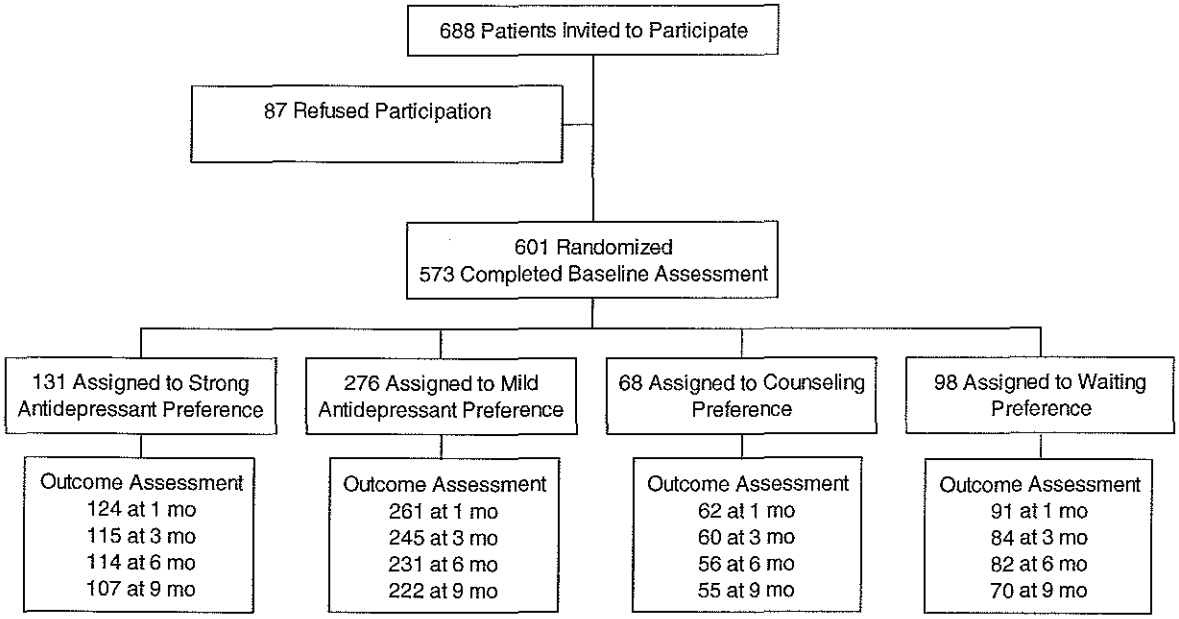


Table 1. Baseline Responses to Patient Treatment Preference Questions

	Antidepressants	Mental Health Counseling	Wait and get over naturally
Response, %			
Definitely acceptable	22.9	25.3	31.6
Probably acceptable	48.2	40.7	51.7
Probably not acceptable	16.1	20.1	11.9
Definitely not acceptable	10.0	12.7	3.1
Don't know	3.0	1.2	1.8

Table 2. Baseline Characteristics of Patients by Preference Group

Variable	Strong antidepressant preference (n=131)	Mild antidepressant preference (n=276)	Counseling preference (n=68)	Waiting Preference (n=98)	Total (n=573)
Age, mean (SD), y *	45.0 (15.3)	44.8 (16.4)	47.2 (12.2)	50.6 (16.8)	46.1 (15.9)
Women, %	82.4	79.7	82.4	70.4	79.1
Race, % **					
White	90.1	87.7	70.6	73.5	83.8
Black	9.2	9.4	22.1	23.5	13.3
Other	0.8	2.9	7.3	3.0	3.0
Depressive d/o diagnosis, % **					
Major depression/bipolar d/o	34.4	30.1	36.8	30.6	31.9
Minor depression	4.6	8.3	8.8	10.2	7.9
Double depression/dysthymia	51.2	54.4	36.8	33.7	48.0
None	9.9	7.3	17.7	25.5	12.2
Past history of depression treatment, % **	44.3	35.9	25.0	12.2	32.5
Anxiety score, mean (SD)	2.18 (0.7)	2.11 (0.8)	1.98 (0.8)	1.96 (0.9)	2.09 (0.8)
Chronic Disease Score, median (range)	1 (0-9)	1 (0-9)	1 (0-9)	1 (0-14)	1 (0-14)
No alcohol last mo., %	54.2	51.5	55.9	65.3	55.0
SSRI randomized, %					
Fluoxetine	31.3	33.5	45.0	31.0	33.7
Paroxetine	31.3	31.0	31.7	42.9	33.0
Sertraline	37.4	35.5	23.3	26.2	33.3
Health care resource utilization, median (range)					
Primary care visits, last 3 mo	1 (0-30)	1 (0-10)	1 (0-11)	1 (0-6)	1 (0-30)
Psychiatrist visits, last 3 mo	0 (0-5)	0 (0-12)	0 (0)	0 (0-1)	0 (0-12)
Mental health visits, last 3 mo	0 (0-15)	0 (0-13)	0 (0-3)	0 (0-3)	0 (0-15)
ER visits for mental health, last 3 mo	0 (0-20)	0 (0-2)	0 (0-2)	0 (0)	0 (0-20)
Hospital days for mental health, last 12 mo	0 (0-6)	0 (0-30)	0 (0)	0 (0)	0 (0-30)

* $P < 0.05$; P-values determined by oneway ANOVA or Kruskal-Wallis test for continuous variables; Pearson's chi-square for categorical variables.

** $P < 0.0001$; P-values determined by oneway ANOVA or Kruskal-Wallis test for continuous variables; Pearson's chi-square for categorical variables.

Table 3. Mean (SD) SCL-20 Scores by Preference Group*

Group	Baseline	1 month	3 months	6 months	9 months
Strong antidepressant preference	1.86 (0.76)	1.19 (0.71)	0.96 (0.67)	0.78 (0.66)	0.75 (0.63)
Mild antidepressant preference	1.68 (0.66)	1.09 (0.62)	0.95 (0.68)	0.92 (0.66)	0.82 (0.64)
Counseling preference	1.52 (0.74)	0.96 (0.62)	0.81 (0.56)	0.85 (0.66)	0.79 (0.71)
Waiting preference	1.43 (0.82)	0.92 (0.62)	0.82 (0.71)	0.73 (0.60)	0.68 (0.60)
P-value**	0.0001	0.0079	0.2056	0.0947	0.4596

* SCL-20 indicates the Symptoms Checklist 20; lower scores indicate fewer depressive symptoms.
** Determined using oneway ANOVA.

Figure 2. Mean SCL-20 Scores by Preference Group

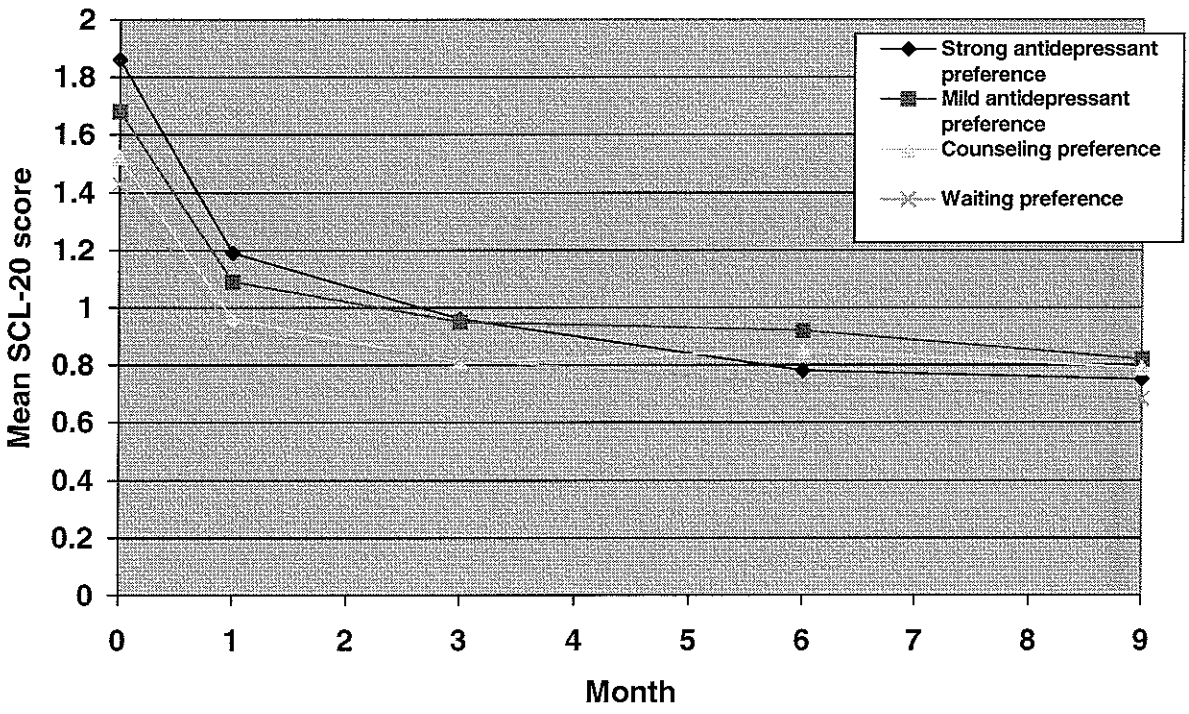


Table 4. Mean (SD) MCS-12 Scores by Preference Group*

Group	Baseline	1 month	3 months	6 months	9 months
Strong antidepressant preference	28.3 (10.6)	41.0 (11.1)	45.4 (11.0)	48.5 (9.5)	49.6 (9.7)
Mild antidepressant preference	32.4 (10.5)	42.9 (10.1)	45.9 (10.8)	46.3 (10.3)	47.7 (9.7)
Counseling preference	36.2 (12.4)	47.2 (9.8)	49.4 (10.1)	48.2 (10.9)	50.7 (9.9)
Waiting preference	36.7 (13.0)	46.3 (10.7)	48.5 (11.3)	48.5 (10.9)	49.3 (10.9)
P-value**	< 0.0001	0.0001	0.0340	0.1479	0.1272

* MCS-12 indicates the Medical Outcomes Survey 12-Item Short-Form Health Survey Mental Component Summary; higher scores indicate better functional status.
** Determined using oneway ANOVA.

Figure 3. Mean MCS-12 Scores by Preference Group

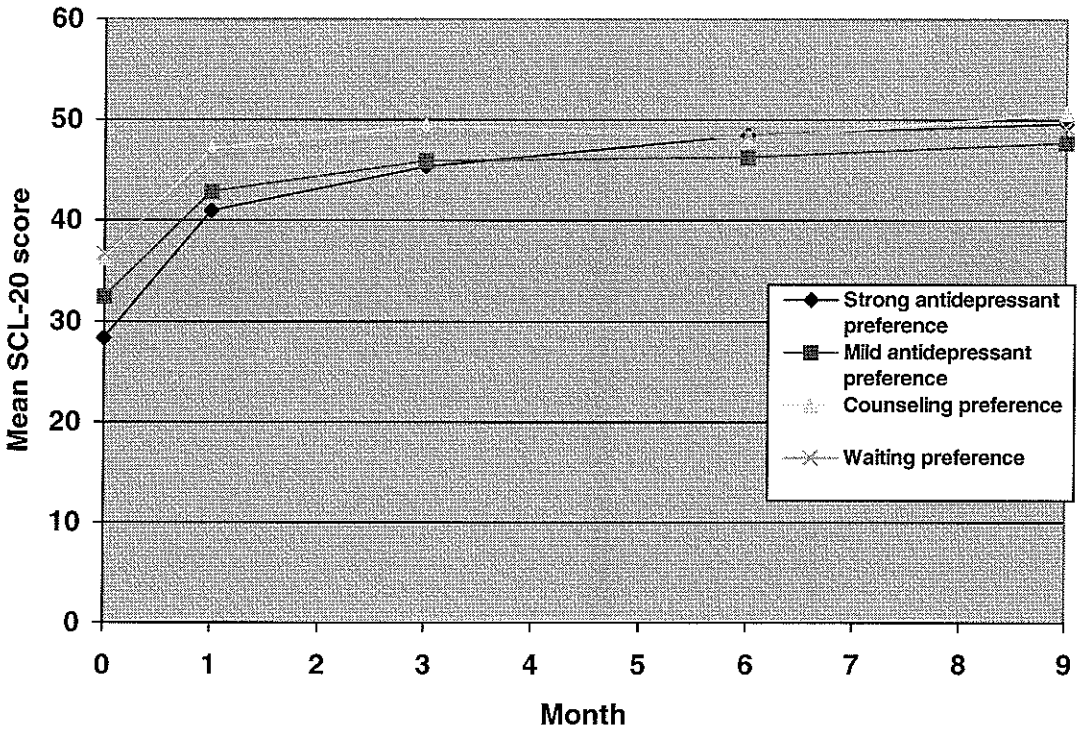


Table 5. Mean (SD) Change in SCL-20 Scores From Baseline by Preference Group*

Variable	1 month	3 months	6 months	9 months
Strong antidepressant preference	-0.65 (0.6)	-0.89 (0.8)	-1.09 (0.8)	-1.10 (0.8)
Mild antidepressant preference	-0.59 (0.6)	-0.72 (0.7)	-0.75 (0.7)	-0.87 (0.7)
Counseling preference	-0.60 (0.7)	-0.72 (0.6)	-0.61 (0.7)	-0.73 (0.8)
Waiting preference	-0.48 (0.7)	-0.62 (0.8)	-0.72 (0.7)	-0.75 (0.8)

* SCL-20 indicates the Symptoms Checklist 20; lower scores indicate fewer depressive symptoms.

Figure 4. Mean Change in SCL-20 Scores from Baseline by Preference Group

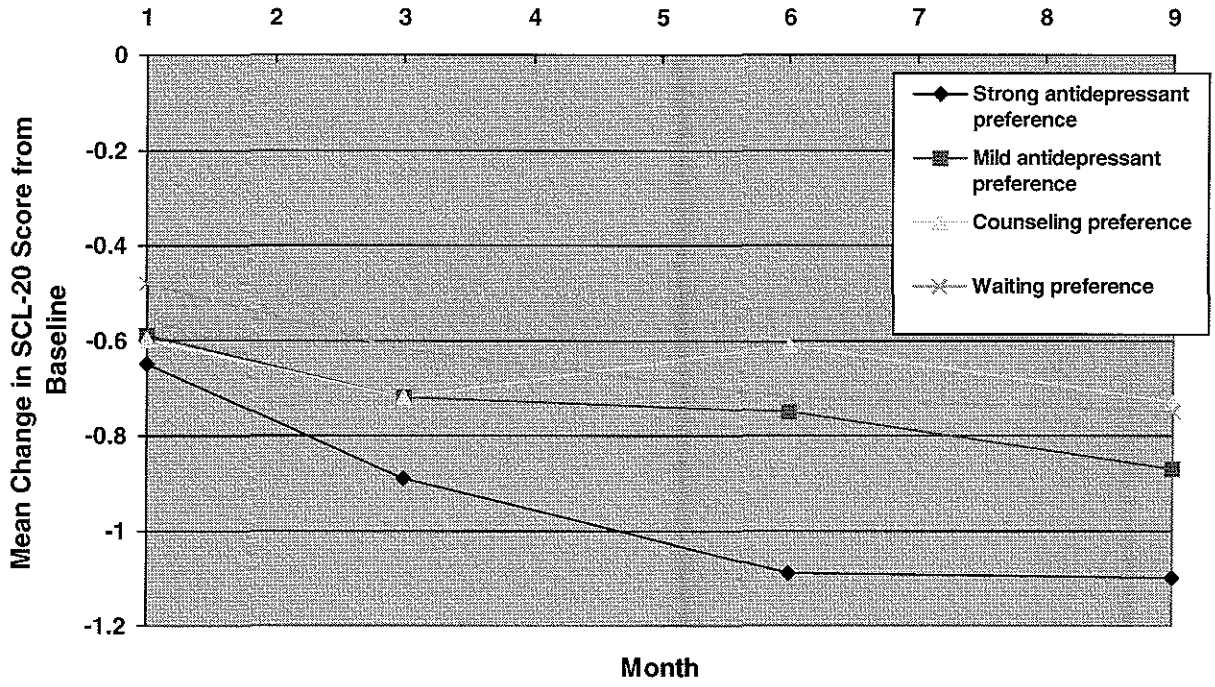


Table 6. Mean (SD) Change in MCS-12 Scores From Baseline by Preference Group*

Variable	1 month	3 months	6 months	9 months
Strong antidepressant preference	12.4 (10.4)	16.9 (12.1)	20.3 (13.2)	21.1 (13.5)
Mild antidepressant preference	10.6 (9.5)	13.4 (12.2)	13.5 (11.4)	15.3 (11.4)
Counseling preference	11.7 (11.0)	13.2 (11.1)	10.9 (11.8)	14.2 (12.6)
Waiting preference	10.2 (10.9)	12.5 (13.4)	11.9 (13.5)	11.9 (13.5)

* MCS-12 indicates the Medical Outcomes Survey 12-Item Short-Form Health Survey Mental Component Summary; higher scores indicate better functional status.

Figure 5. Mean Change in MCS-12 Scores from Baseline by Preference Group

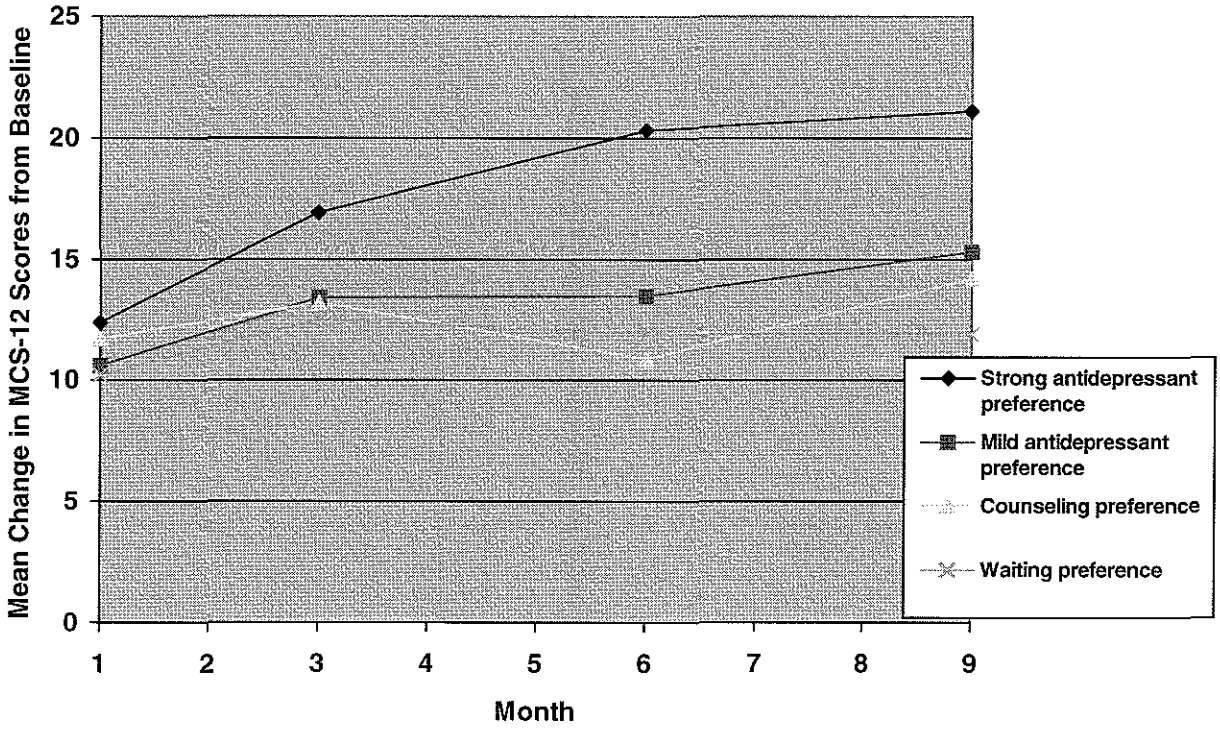
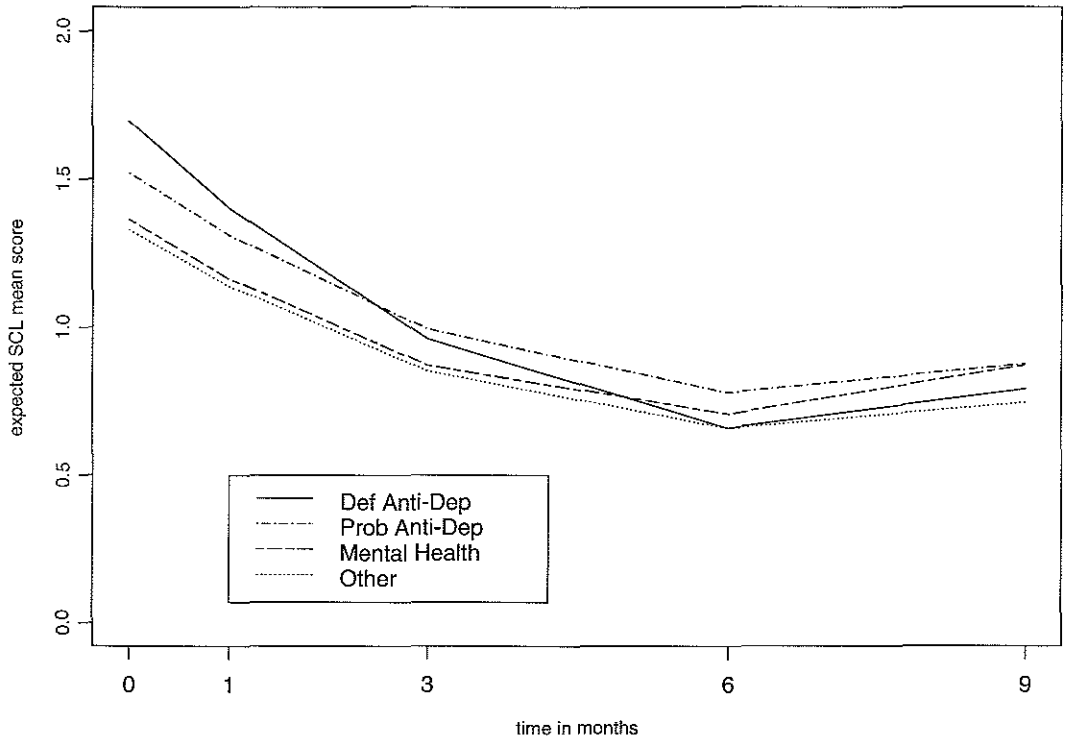
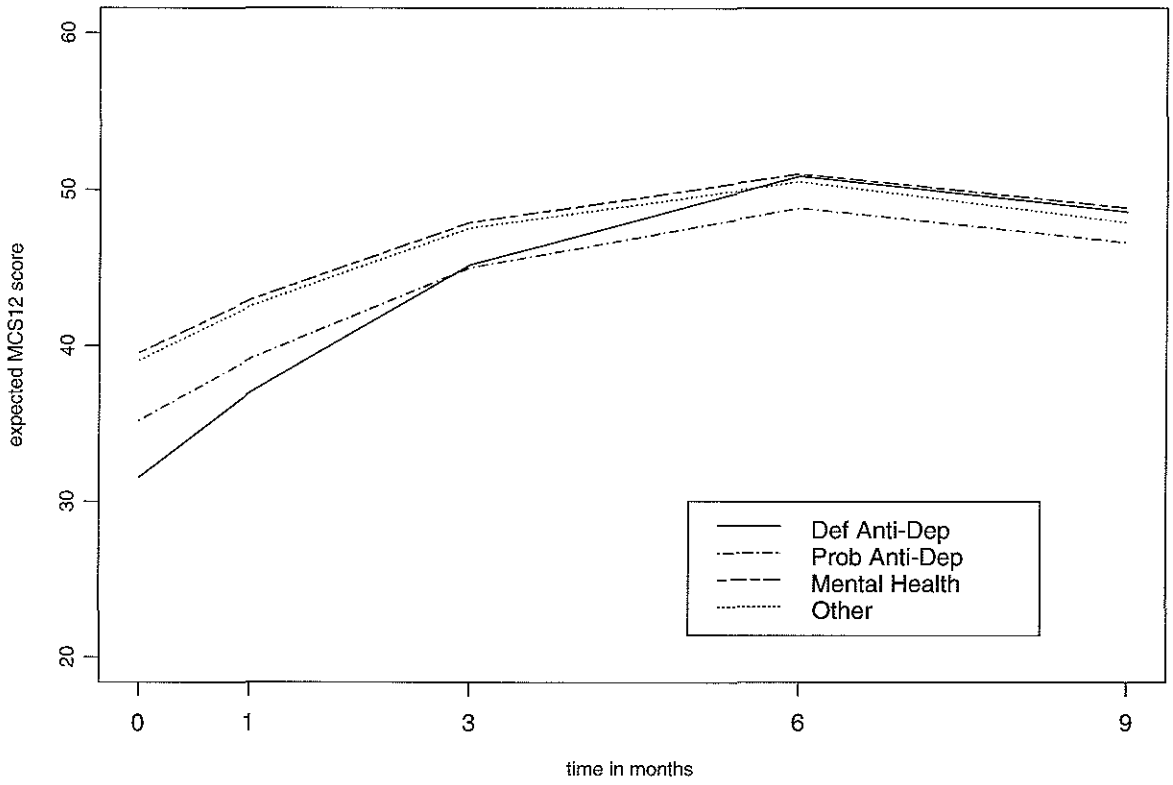


Figure 6 Predicted Mean SCL-20 Scores Based on Linear Mixed-Effects Model*



* SCL-20 indicates the Symptoms Checklist 20; lower scores indicate fewer depressive symptoms.

Figure 7 Predicted Mean MCS-12 Scores Based on Linear Mixed-Effects Model*



* MCS-12 indicates the Medical Outcomes Survey 12-Item Short-Form Health Survey Mental Component Summary; higher scores indicate better functional status.

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