Depression, Health-Related Quality of Life, and Medical Cost Outcomes of Receiving Recommended Levels of Antidepressant Treatment

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BACKGROUND. We evaluated depression severity, health-related quality of life (HRQL), and medical cost outcomes of primary care patients receiving recommended and less-than-recommended levels of antidepressant treatment.

METHODS. We performed a secondary analysis of clinical trial data from primary care clinics in a staff-model managed care organization. The trial included patients with *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R)* criteria for major depression who were starting antidepressant treatment. The primary outcomes measures used were the 17-item Hamilton Depression Rating Scale (HDRS), Hopkins Symptom Checklist depression scores, the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) mental and physical component summary scores, and the total outpatient and inpatient medical costs.

RESULTS. Of 358 patients starting antidepressant treatment, 195 (54.5%) received doses recommended by the Agency for Health Care Policy and Research for 90 days or more. Mean HDRS score decreased from 14.1 to 8.8 in patients receiving less-than-recommended treatment and decreased from 13.8 to 8.9 in patients with minimum recommended treatment ($P = .761$). No significant differences in improvement of HRQL outcomes during 6 months were observed between patients receiving recommended or less-than-recommended antidepressant therapy. Mean total medical costs over 6 months for patients taking the recommended levels of antidepressant treatment were $1872±140 compared with $2622±413 for patients taking less-than-recommended treatment ($P = .032$). The differences in total medical costs were attributable to significantly lower nonmental health-related inpatient costs in the recommended antidepressant treatment group ($104 vs $785, $P = .004$).

CONCLUSIONS. Patients receiving minimum recommended levels of antidepressant therapy for 3 months showed improvement in depression severity and HRQL comparable with patients receiving less-than-recommended treatment. Patients receiving minimum recommended treatment had lower total costs and nonmental health–related inpatient costs. Antidepressant treatment in primary care patients may have the greatest impact on the frequency of health care visits and on costs for medical conditions and impairments.

KEY WORDS. Depression; antidepressants; health care costs; quality of life. (*J Fam Pract 1998; 47:446-452*)

Depression is an often disabling psychiatric disorder frequently seen in primary care practice. It is associated with serious impairment of health-related quality of life (HRQL), significant disability,[1-4] and increased medical costs.[5,6] Research on the treatment of depression in primary care settings has demonstrated problems with the detection and diagnosis of depression.[7-9] To address this issue, the Agency for Health Care Policy and Research (AHCPR) Depression Guideline Panel developed guidelines for the diagnosis and clinical management of depres-

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sion in primary care practice.[10]

Primary care patients often receive lower doses of antidepressant medications, are followed up less frequently, have less adequate monitoring of outcomes, and discontinue treatment earlier than patients seen by mental-health specialists. Few primary care patients with depression receive adequate doses of antidepressant medications for 3 months.[11-17] Wells and colleagues,[17] using Medical Outcomes Study data, found that 61% of depressed outpatients treated with antidepressants received therapeutic doses, based on minimum therapeutic dosages. Simon and coworkers[18] found that 56% of 88 patients starting antidepressant treatment received adequate doses for 30 days. No differences were observed at 4 months in depression symptoms between patients given a recommended antidepressant treatment and those who were not.

Significant numbers of primary care patients with depression do not receive minimum recommended levels

of antidepressant treatment. There are few published data on the short-term or long-term impact of recommended treatment compared with less-than-recommended treatment on depression symptoms, HRQL, and health care costs. Antidepressant dosage and duration are based primarily on 6- to 8-week clinical trials conducted in psychiatric specialty settings that have different patient populations from those seen in primary care. It is uncertain whether antidepressant treatment regimens developed in psychiatric specialty settings are appropriate for and generalizable to primary care patients. Follow-up studies of primary care patients indicate less depression severity and better short-term outcomes than with specialty-treated patients.[19,20] Simon and colleagues[18] found no difference in 4- to 7-month depression outcomes between low-intensity and high-intensity antidepressant treatment, although the high-intensity group demonstrated a greater percentage of responders than did the low-intensity group. There are no data available for antidepressant effects on HRQL or total health care costs based on whether patients receive recommended or less-than-recommended levels of antidepressant treatment.

This report summarizes the depression, HRQL, and medical cost outcomes of patients who were enrolled in a naturalistic clinical trial of antidepressant treatment in primary care[21] and were receiving minimum recommended antidepressant treatment, according to the AHCPR depression practice guidelines.[10]

METHODS

Our study is a secondary analysis of data from a naturalistic, randomized clinical trial of antidepressant treatment in primary care that was performed from 1992 to 1995.[21] Patients with depression were identified by physicians practicing in selected primary care clinics of the Group Health Cooperative (GHC) of Puget Sound. GHC is a staff-model managed care organization serving approximately 400,000 members, and GHC enrollment is representative of the Seattle-area general population. The research protocol was approved by GHC's institutional review board, and patients provided written consent before entering the study.

Physicians referred patients older than 18 years who were beginning antidepressant treatment for depression to the study if the patient and the physician agreed to random assignment to medication. Eligibility was based on physician-diagnosed depression. Exclusion criteria included use of antidepressant medications in the previous 90 days; current alcohol abuse (defined as greater than one positive response to the CAGE questionnaire[22] and average consumption of more than 10 drinks per week); current psychotic symptoms or history of mania according to modules from a structured diagnostic interview for the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R)*;[23] recent use of lithium or antipsychotic medications; current pregnancy; or contraindications to any of the study medications. At baseline, all patients were evaluated for *DSM-III-R* criteria for major depression and dysthymia using the depression module of the structured diagnostic interview. Patients were stratified by presence or absence of current major depression and were randomly assigned to start treatment with either desipramine, imipramine, or fluoxetine. Patients and physicians were not blinded to treatment, and they made all decisions about antidepressant treatment according to usual practice.

CLASSIFICATION OF MINIMUM RECOMMENDED ANTIDEPRESSANT TREATMENT

For these analyses, all patients with *DSM-III-R* criteria for major depression (67% of original study sample) were eligible regardless of antidepressant treatment. Patients were classified into the recommended antidepressant treatment group if they received at least the minimum levels in the recommended range of doses of antidepressant medications based on AHCPR guidelines[10] for at least 3 months. (The minimum recommended dosages were 10 mg per day for fluoxetine, 75 mg per day for imipramine, and 75 mg per day for desipramine.) Computerized pharmacy records were used to classify patients into 2 groups: those receiving minimum recommended levels of antidepressant treatment (MRT) and those receiving less-than-recommended levels of antidepressant treatment (< MRT), on the basis of previously developed algorithms.[15-18] These records contain information on all antidepressant medications dispensed at GHC pharmacies, including medication dose and rates of refill. Surveys of GHC members demonstrate that more than 95% of prescriptions are filled at GHC pharmacies.[25] For the clinical trial, copayments for antidepressant medications were waived to encourage use of GHC pharmacies; therefore, complete data on antidepressant medication prescription refills were expected. No data were collected on reasons for less-than-recommended treatment.

MEASURES

This study included depression severity measures, HRQL measures, and total medical costs. Assessments were performed at baseline and at 1 month, 3 months, and 6 months by interviewers blinded to treatment assignment, using in-person (22%) or telephone (78%) interviews.

Clinical severity. Depressive symptom severity was measured using the Hamilton Depression Rating Scale (HDRS),[26,27] and clinical symptoms were assessed with the Hopkins Symptom Checklist (SCL) depression and anxiety scales.[28] The 17-item version of the HDRS was administered as a structured interview. Simon and colleagues[29] found excellent agreement between telephone and in-person administration of the HDRS and the SCL depression scales.

Health-related quality of life. The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) was used to measure patient functioning and well-being.[30] The SF-36 has excellent internal consistency and test-retest reliability as well as good construct and known-groups validity.[30] The SF-36 has been used in numerous studies in the primary care population and in depressed and other chronic disease populations. The mental component and physical component summary scores derived from the SF-36 scales[31] were used in these analyses.

Medical costs. Data were collected on medical service utilization at GHC facilities and on the use of non-GHC health services. GHC's administrative systems were used to provide data on units of GHC medical service use, such as outpatient physician visits, medications, and laboratory tests, and actual accounting costs were assigned to units of service. During each follow-up assessment, patients were asked questions about the use of out-of-plan health services, and the relevant GHC costs were assigned to these services. Total medical costs, total outpatient costs, and total inpatient costs were calculated for 6 months after the start of antidepressant therapy. Inpatient and outpatient costs were subdivided into mental health related and nonmental health related.

Disease severity. The chronic disease score (CDS), based on computerized pharmacy data, was constructed as an indicator of chronic illness morbidity.[32,33] The CDS correlates strongly with the physician's perception of chronic medical problems and is associated with mortality, hospital admissions, and the utilization and costs of health care services.[33]

DATA ANALYSIS

This is a secondary analysis of data collected in a naturalistic clinical trial. The data from the 3 antidepressant treatments groups were pooled, since Simon and coworkers[21] found no statistically significant differences between the groups on measures of depression severity, HRQL, total medical costs, or clinical outcome, using an analysis based on initial treatment assignment. For the baseline between group comparisons, chi-square tests were used to compare patients who received MRT and < MRT for categorical variables and *t* tests were used to evaluate differences for continuous variables. Between-group comparisons of depression severity and HRQL outcomes after 1 month, 3 months, and 6 months of follow-up were made using analysis of covariance models, adjusting for baseline scores, age, sex, chronic disease scores, previous depressive episodes, and previous antidepressant therapy. We used actual (untransformed) and log-transformed total and outpatient medical costs and rank-transformed inpatient medical costs in the between-group comparisons. Analysis of covariance models was used to compare the 6-month medical costs between groups, adjusting for total medical costs for 6 months before study entry, age, sex, chronic disease score, previous depressive episodes, and previous anti-

depressant therapy. A two-tailed $P = .05$ was used to assess statistical significance, and no adjustments were made for multiple comparisons.

RESULTS

At study entry, 358 patients (67%) met *DSM-III-R* criteria for major depressive disorder. The study sample was 71% women, and the mean age was 41.5 years (standard deviation [SD] = 12.5).The baseline mean HDRS score was 13.9 (SD = 2.4) and the mean SCL depression scale score was 2.29 (SD = .70). Seventy-eight percent of the patients reported one or more previous depressive episodes, and 33% reported previous treatment with an antidepressant medication. Patients with complete follow-up assessments did not differ significantly from those not completing follow-up on age, sex, or baseline depression severity.[21]

ANTIDEPRESSANT TREATMENT

One hundred ninety-five patients (54.5%) received at least 90 days of the minimum recommended levels of antidepressant medication during the 6-month study, with the remaining 163 patients classified as receiving < MRT. Patients receiving MRT did not differ significantly from those taking < MRT with regard to age, previous depressive episodes, or previous antidepressant treatment. More men (64%) than women (50%) received MRT ($P = .016$). Mean chronic disease scores were slightly lower for patients with MRT than with those with < MRT (921.5 vs 1016.6, $P = .372$).

CLINICAL SEVERITY

Baseline mean HDRS scores were not statistically significantly different (MRT = 13.8, < MRT = 14.1, $P = .339$). The baseline mean SCL depression score for the group receiving MRT was 2.31 (SD = .67) and 2.25 (SD = .73) for the < MRT group ($P = .433$). There were no differences between the 2 groups on baseline mean SCL anxiety scales scores ($P = .475$). No statistically significant differences were observed on HDRS scores between the MRT group and the < MRT group after 1 month, 3 months, and 6 months of follow-up (Figure 1). The mean HDRS score in the < MRT group decreased from 14.1 (standard error [SE] = .19) to 8.8 (SE = .39) at 6 months. The mean HDRS score for patients in the MRT group decreased from 13.8 (SE = .17) to 8.9 (SE = .33) over this same period. Mean SCL depression scores decreased in both groups and were not statistically significantly different at 1 month, 3 months, and 6 months (Figure 2). SCL depression scores demonstrated similar improvements in both groups.
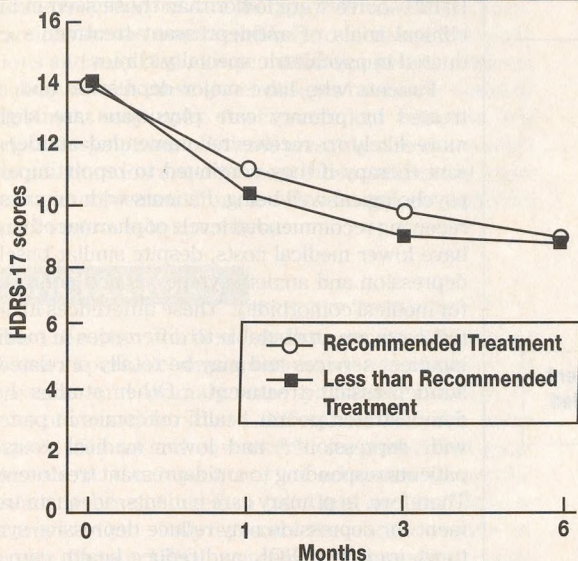
HEALTH-RELATED QUALITY OF LIFE

At baseline, patients receiving MRT had a similar mean mental component summary score (mean = 25.7, SD = 7.5) compared with those patients getting < MRT (mean = 26.3, SD = 9.3, $P = .512$). Mean physical component summary scores were 50.9 (SD = 11.2) and 50.4 (SD = 10.3) for the

FIGURE 1

Course of HDRS-17 scores for primary care patients receiving recommended and less than recommended antidepressent treatment.

HDRS-17 denotes the 17-item Hamilton Depression Rating Scale.

MRT and < MRT groups, respectively (P = .706). No statistically significant differences in mean mental component summary scores between the 2 patient groups were observed during 6 months of observation (Figure 3). Mean mental component summary scores at 6 months were 45.2 (SE = .88) for MRT patients and 47.7 (SE = .98) for < MRT patients (P = .507). No statistically significant differences between the 2 groups were observed in mean physical component summary scores during 6 months of follow-up.

MEDICAL COSTS

We compared the total and disaggregated medical costs during 6 months for the 2 patient groups (Table). Mean total medical costs were $2622 (SE = $413) for the < MRT group and $1872 (SE = $140) for the MRT group (P = .032). The costs of outpatient treatment were comparable between the 2 groups. Most of the differences between the treatment groups were because of inpatient medical costs (P = .006). Patients with < MRT had mean nonmental health–related hospital costs that were 7 times greater than the mean hospital costs for patients with MRT (P = .004).

DISCUSSION

In this group of primary care patients starting antidepressant treatment for major depressive disor-

der, 55% received pharmacotherapy consistent with the minimum level of the range of antidepressant dosages and duration as recommended by the AHCPR for treatment of depression in primary care. Men were more likely to receive MRT, regardless of depression severity. Pharmacologic treatment intensity was not associated with baseline depression severity, self-reported depression or anxiety symptoms, general psychological well-being, or physical functioning. After adjusting for baseline differences, patients receiving MRT reported slightly less improvement in SF-36 psychological well-being at 6 months compared with patients with < MRT. No differences were observed between the 2 groups on the depression severity measures.

The medical costs for < MRT patients were about $750 higher than for MRT patients. The differences were primarily because of significantly higher inpatient costs for medical conditions. These results were consistent with research demonstrating that patients responding to antidepressant treatment also had lower total medical costs and lower nonmental health–related costs.[34,35] The variations in total costs were not attributable to comorbid anxiety, since no differences were observed in anxiety scale scores between the 2 groups; instead these variations might be because of preexisting differences in medical comorbidities between the groups. However, all comparisons of medical costs controlled for these differences using the chronic disease score. There is evidence that comorbid depression is associated with poorer out-

FIGURE 2

Course of SCL depression scores for primary care patients receiving recommended and less than recommended antidepressant treatment.
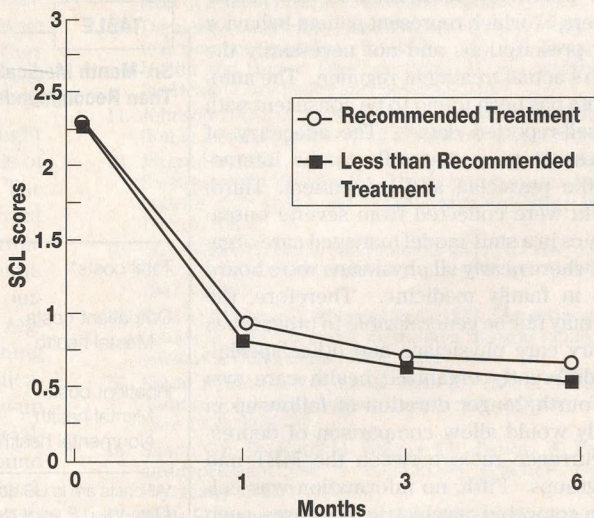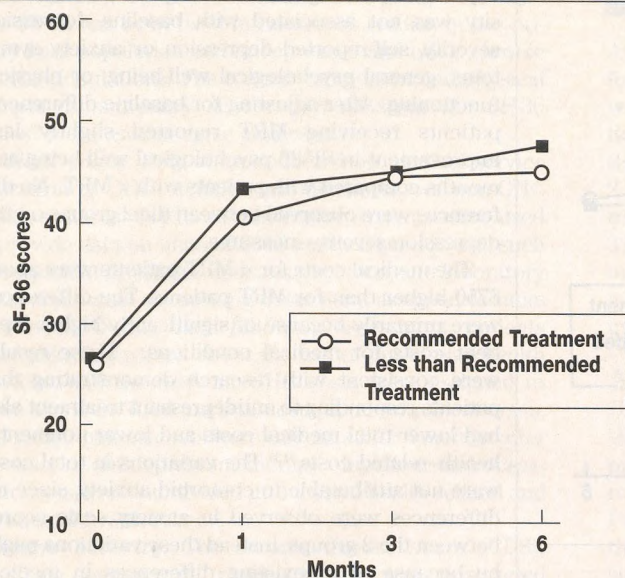

SCL denotes Hopkins Symptom Checklist.

FIGURE 3

Course of SF-36 mental component summary scores for primary care patients receiving recommended and less than recommended antidepressant treatment.

SF-36 denotes the Medical Outcomes Study 36-Item Short-Form Survey.

comes for chronic medical illnesses,[35-38] which may explain the greater costs in the < MRT group.

Several potential study limitations should be kept in mind when interpreting these results. First, the definition of MRT reflected minimum dose and duration; other definitions might reach different conclusions. Second, we analyzed pharmacy refill records, like other researchers,[15,18] which represent patient behavior in filling prescriptions and not necessarily the physician's actual treatment regimen. The automated data has been found to be consistent with patient self-reported data.[39] The adequacy of antidepressant treatment reflects the interaction of the physician and the patient. Third, these data were collected from several outpatient clinics in a staff-model managed care organization where nearly all physicians were board certified in family medicine. Therefore, the findings may not be generalizable to other types of primary care physicians and other specialties or differently organized health care systems. Fourth, longer duration of follow-up in this study would allow comparison of depression recurrence rates between the MRT and < MRT groups. Fifth, no information was collected on comorbid psychiatric diagnoses, such as anxiety disorders or somatization disorders; the presence of comorbid anxiety might have

an impact on patient outcomes and medical costs.[40] Finally, although these patients met *DSM-III-R* criteria for major depressive disorder, the HDRS scores were lower than those seen in most clinical trials of antidepressant treatments conducted in psychiatric specialty clinics.

Patients who have major depression and are treated by primary care physicians are slightly more likely to receive recommended antidepressant therapy if they continued to report impaired psychological well-being. Patients with depression receiving recommended levels of pharmacotherapy have lower medical costs, despite similar baseline depression and anxiety symptoms and controlling for medical comorbidity. These differences in medical costs are attributable to differences in medical inpatient services and may be totally unrelated to antidepressant treatment. Other studies have demonstrated poorer health outcomes in patients with depression[35-38] and lower medical costs in patients responding to antidepressant treatment.[34,35] Therefore, in primary care patients, adequate treatment for depression may reduce depressive symptoms, improve HRQL, and reduce health care utilization for medical conditions. This finding needs to be confirmed and explored in future prospective studies.

Decisions about treatment are influenced by physician-patient interaction and observations about the course of the patient's depressive episode. Recent research by Lin and colleagues[41] suggests that educational messages from physicians to their patients have an important influence on patient adherence to antidepressant therapy. Patients with higher initial severity of depression, persistent symptoms of depression, and

TABLE

Six-Month Medical Costs for Patients with Recommended and Less Than Recommended Antidepressant Treatment

	Recommended Treatment Mean (SD)	Less than Recommended Treatment Mean (SD)	P†
Total costs*	1872 (1949)	2622 (5270)	.032
Outpatient costs	1690 (1417)	1690 (1763)	.843
Mental health	559 (1018)	529 (849)	.990
Inpatient costs	932 (4035)	182 (1173)	.006
Mental health	60 (637)	147 (1261)	.360
Nonmental health	104 (844)	785 (3538)	.004

*All costs are in US dollars.
†Two-tailed P value for treatment intensity from general linear model, adjusting for sex, age, chronic disease score, previous depression episode, previous antidepressant treatment, and total medical costs in the 6 months before study entry.

impaired functioning and well-being are more likely to continue antidepressant medications or have their dosages increased. For patients who are demonstrating a response to antidepressant therapy, even at < MRT, primary care physicians may be unlikely to increase their medications and may discontinue medications early. Patients who recover with these lower dosages or shorter duration of treatment may make fewer visits and complain less about their symptoms. Patients prescribed recommended doses and duration may represent those patients not experiencing improvement from low-dose treatment and who seem to require more treatment.

CONCLUSIONS

These results confirm documented differences between expert recommendations on the treatment of depression and primary care physician practice.[11-18] The explanation for these differences may be more complex. Simon and coworkers[18] suggested that judgments about the inadequacy or adequacy of antidepressant treatment need to take into account patient outcomes. Our study extends the earlier results to consider patient HRQL outcomes and medical costs. The findings demonstrate no differences in HRQL outcomes but do show significant differences in medical costs by intensity of antidepressant treatment in primary care patients with major depressive disorder. In this study, adequate antidepressant treatment actually reflects the lowest dosages in the AHCPR-recommended ranges prescribed for 3 months, and if the patient has not improved at this dosage then clinically it is not adequate treatment. Low-intensity treatment that achieves improvements in depressive symptoms and that has a positive impact on the use of medical services may be appropriate. Patients fitting into this subgroup may not necessarily gain more with intensive antidepressant treatment. It is uncertain whether there are long-term consequences in depression recurrence rates associated with < MRT.

The treatment of depression in primary care might be improved with greater attention to matching levels of antidepressant treatment with patient outcomes. The patient's previous depression history, such as recurrent depressive episodes and previous response to pharmacologic treatment, must also be taken into account. Given the large group of patients with successful outcomes despite low-intensity antidepressant therapy, regular follow-up and measurement of patient functioning and well-being and subsequent adjustments in medication doses seem reasonable. In primary care, follow-up and outcome monitoring is less frequent than in specialty practice; for example, Simon and colleagues[21] found that the average patient was seen twice by their physician during the initial 8 weeks of antidepressant treatment. More frequent and long-term follow-up and monitoring of response to treatment might reduce depression

severity and improve patient HRQL and treatment for medical conditions in patients with comorbid depression. A more targeted approach to the antidepressant regimen, with attention to patient outcomes and medical comorbidity, may improve matching patient subgroups to appropriate treatments and increase the efficiency of health care resources in producing successful patient health outcomes.

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