Relapse of Depression in Primary Care

Rate and Clinical Predictors

Elizabeth H. B. Lin, MD, MPH; Wayne J. Katon, MD; Michael VonKorff, ScD; Joan E. Russo, PhD; Greg E. Simon, MD, MPH; Terry M. Bush, PhD; Carolyn M. Rutter, PhD; Edward A. Walker, MD; Evette Ludman, PhD

Objective: To determine the clinical predictors and rate of relapse for major depression in primary care.

Design: A cohort study of subjects in 2 randomized trials of depressed patients diagnosed and prescribed antidepressant medicine by primary care physicians. Baseline, 7-month, and 19-month assessments were conducted.

Setting: A large primary care clinic of a staff-model health maintenance organization.

Patients: Two hundred fifty-one primary care patients who did not satisfy *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition* (*DSM-III-R*) criteria for major depression at 7 months.

Main Outcome Measures: Relapse was defined as (1) satisfying *DSM-III-R* criteria for major depression at 19 months, *or* (2) reporting an interval episode of 2 weeks or more of depressed mood and symptoms between 7 and 19 months. Predictors examined included demographic characteristics, medical comorbidity, disability, and psychological symptoms. Depressive symptoms were measured by Inventory of Depressive Symptoms and Hopkins Symptoms Checklist.

Results: Of the patients, 37.1% reported relapse of depression in the 12-month relapse-risk period. The 2 major risk factors associated with relapse were (1) persistence of subthreshold depressive symptoms 7 months after the initiation of antidepressant therapy (odds ratio, 3.3; 95% confidence interval, 2.74-3.93) and (2) history of 2 or more episodes of major depression, or chronic mood symptoms for 2 years (odds ratio, 2.1; 95% confidence interval, 1.41-2.76). Patients with both risk factors were approximately 3 times more likely to relapse than patients with neither.

Conclusions: The relapse rate among primary care patients treated for depression approached that of specialty samples, with more than one third reporting relapse in 1 year. Clinical characteristics can help target high-risk patients for relapse prevention efforts.

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From the Center for Health Studies (Drs Lin, VonKorff, Simon, Bush, Rutter, and Ludman) and Northgate Medical Center (Dr Lin), Group Health Cooperative of Puget Sound, Seattle, Wash; and the Department of Psychiatry and Behavioral Sciences, School of Medicine, University of Washington, Seattle (Drs Katon, VonKorff, Russo, Simon, and Walker).

RESEARCH DURING the last decade has changed our understanding of the natural course of major depression. Depression is no longer viewed as an acute illness with good long-term prognosis. Instead, its course is often relapsing and remitting and can be chronic in approximately 10% of patients.[1-4] Since depression is so common, with 1 in 4 women and 1 in 6 men in the United States suffering from a major depressive episode in their lifetime,[5] its recurrent and chronic nature has significant public health implications. Half to three quarters of patients with a single episode will have another episode in their lifetime.[6] Among persons who have had at least 2 episodes of major depression, 70% to 90% will have a third episode.[7] Moreover, patients with recurrent depression are overrepresented in the prevalence pool of clinical populations. Recent research has shown that two thirds of patients with major depression treated by their primary care physician had experienced 2 or more previous depressive episodes.[8,9] These substantial relapse rates are especially pertinent for the general health care setting, since depressed patients are most likely to seek help from their primary care physicians.[10]

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PATIENTS AND METHODS

This is a cohort follow-up study of 2 sequential randomized trials, conducted between February 1, 1992, and June 30, 1994, to evaluate collaborative management of depressed primary care patients by their family physicians and on-site mental health consultants. The methods and the interventions of the 2 collaborative care studies have been described in detail in previous articles reporting the effects of the interventions on depression outcomes.[9,20] The Human Subjects Committees of Group Health Cooperative of Puget Sound (GHC) and the University of Washington Medical School, Seattle, had approved the procedures and interventions.

SETTING

This study was carried out at the Northgate Medical Center of GHC, Seattle. The Northgate Medical Center is a primary care clinic serving the health care needs of approximately 28 000 adults and children. These enrollees had access to family physicians, pediatricians, physicians' assistants, and nurse practitioners for their primary health care needs. Every family physician (N = 22) at the clinic participated, and all were board certified. The GHC is a health maintenance organization that serves about 400 000 residents in western Washington State who are similar to the surrounding population except for a higher educational level, a greater proportion employed, and less representation from the high and low socioeconomic strata.[21]

SAMPLE SELECTION

The **Figure** illustrates the selection of our study sample. After they gave written informed consent, patients diagnosed by their family physicians as depressed could be referred to 1 of the 2 randomized trials (conducted sequentially) to receive the collaborative care program or usual care. The eligibility criteria included the following: 18 to 80 years of age, diagnosis of definite or probable major depression, a score on the Hopkins Symptoms Checklist (SCL) depression scale of 0.75 or greater,[22] and willingness to take antidepressant medication. Patients were excluded on the basis of alcohol abuse, psychotic symptoms, dementia, pregnancy, terminal illness, language barrier, or plans to disenroll from GHC in the next 12 months. In the first study (psychiatrist-collaboration study), patients were cotreated by their primary care physician and an on-site consulting psychiatrist.[9] In the second study (psychologist-collaboration study), patients were cotreated by their primary care physician and an on-site psychologist who provided education to improve medication adherence as well as a brief cognitive behavioral therapy program and telephone follow-up.[20] Patients in both studies received an educational videotape and 2 pamphlets on depression. All intervention visits were provided during the initial 3 months (acute-phase treatment), with monitoring of medication adherence in the continuation phase. Treatment effects were similar for both studies.[9,20] Each intervention program improved acute-phase treatment of depression in primary care according to Agency for Health Care Policy and Research guidelines.[7] At 4 and 7 months after initiation of treatment, patients with major depression at baseline showed significant improvements in psychological outcomes, patient satisfaction, and adherence to antidepressant therapy. Among the 498 patients referred to the study, 370 patients (74.3%) were randomized, 71 (14.3%) were ineligible, and 57 (11.4%) declined participation. There were 257 patients (69.5%) who completed both the 7- and 19-month follow-up interviews; 5 patients were further excluded because they met *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition*[23] (*DSM-III-R*) criteria for major depression at the 7-month follow-up assessment, and 1 subject had missing data on relapse. Thus, 251 subjects constituted the cohort for this follow-up study.

STUDY DESIGN

Follow-up telephone interviews at 7 and 19 months were used to determine relapse rates and clinical outcomes. Surveyors were blinded to the randomization status of subjects. The 12-month interval between these 2 assessments was designated as the relapse risk period. Relapse was assessed for patients who did not meet *DSM-III-R*[23] criteria for major depression at the 7-month interview. *Relapse* was defined as (1) satisfying *DSM-III-R* criteria for major depression at the 19-month assessment *or* (2) reporting an interval episode between 7 and 19 months. An interval episode was assessed by 2 questions adapted from the National Institute of Mental Health Diagnostic Interview Schedule[24]: (1) During the past year, has there been a period of time when you felt sad, blue, or depressed nearly every day for 2 weeks or more? and (2) During this period did you also have other symptoms such as trouble sleeping, loss of energy, or loss of interest in activities you usually enjoy? Previous research has differentiated relapse from recurrence on the basis of the timing of symptom return.[2,25] Relapse occurs within 6 months after symptom remission, and recurrence appears 6 months or more after symptom remission. Given the timing of the follow-up assessments (7 and 19 months after initiation of pharmacotherapy) and earlier results showing that most of the patients have symptom resolution by 4 months, *relapse* will be used henceforth to refer to both relapse and recurrence.

STUDY MEASURES

Measures of psychological outcomes included the following: (1) the SCL,[22] (2) the Inventory of Depressive Symptoms (IDS),[26] and (3) the NEO Neuroticism Scale (NEO).[27] The SCL is scored on a 0 to 4 scale of severity. Twenty items from the

Efforts to improve care for depression in primary care settings have largely focused on increasing the accuracy of diagnosis and improving acute-phase management.[9,11,12] However, given that the highest relapse rates occur in the first 6 months after stopping pharmacotherapy,[4] improving the continuation and maintenance phases of depression treatment is necessary to decrease the burden of this prevalent disorder.

The National Institute of Mental Health,[6] the World Health Organization,[13] and the Agency for Health Care Policy and Research[7] have all recommended long-term maintenance antidepressant treatment for patients at high risk of relapse or recurrence. The decision to embark on long-term maintenance pharmacotherapy can be difficult for both patients and physicians. Patients have to accept depression as a chronic or relapsing and remitting

depression, vegetative, and anxiety subscales were used (range, 0-80). The SCL has been used in numerous studies of medical patients and was found to have high reliability and validity.[22] The IDS (clinician rated) is a 28-item scale measuring depressive symptoms on a 0 to 3 severity index. It has been found to be correlated highly with a standard scale such as the Hamilton Depression Scale.[28] Since the IDS score represents a continuous measure of depression severity, the original format was modified for telephone interview to allow structured rating of depressive symptoms to determine whether a patient met *DSM-III-R* criteria for major depression. The diagnoses of panic and generalized anxiety disorder were also based on the structured IDS interview. The NEO Neuroticism Scale is a 5-factor inventory covering 60 items.[27] The individual items were scored on a 0- to 4-point scale from strongly disagree to strongly agree. Seven items from the Neuroticism Scale were used in this study (range, 0-28) because these items have been found to predict persistence of depressive symptoms after controlling for depression severity in a large primary care sample.[29] To get meaningful odds ratios, the continuous variables (IDS, SCL, and NEO scores) were dichotomized as high or low. When the distributions were highly skewed, the median value was used to determine the cutoff.

Previous episodes of major depression and a history of more than 2 years of chronic mood symptoms (dysthymic disorder) were assessed by 2 questions listed above that were based on the National Institute of Mental Health Diagnostic Interview Schedule.[24] However, data were missing in 9.2% of the sample for the question on previous episodes of major depression, and an additional 13.1% had missing data for chronic mood symptoms. Consequently, 22.3% of the sample had missing data on either one of these 2 measures. Since there was a high degree of overlap between these 2 measures (83.2% of patients with dysthymia reported 2 or more previous episodes of major depression), they were combined. A history of frequent recurrences of depression, and chronicity of depressive symptoms are indicators of a less favorable prognosis.[2,4,6,13,29]

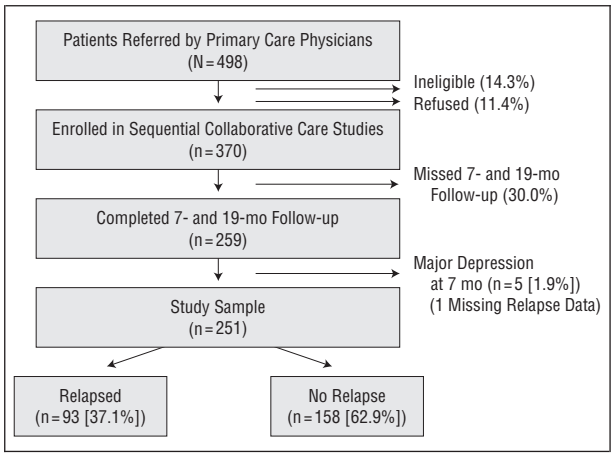
Disability was measured by 5 dichotomous questions on the Activities of Daily Living scale of the Short Form–36[30] and 1 question assessing the number of days patients reported limiting their daily activities because of health problems in the previous 3 months. Coexisting chronic medical illness was assessed by the Chronic Disease Score, which is based on patients' use of prescription medications during a 6-month period.[31] The Chronic Disease Score has been found to have high stability during a 1-year period and to be highly correlated with physician rating of physical disease, hospitalization, and mortality during a 1-year period.

STATISTICAL ANALYSES

We first assessed potential bias caused by unavailability for follow-up in the study sample by comparing the patients who completed the baseline, 7-month, and 19-month follow-ups with those who did not complete all the assessments. We used χ^2 tests to compare categorical variables and 2-tailed t tests for normally distributed continuous variables. Nonparametric median tests were used for visit data and the number of days with limited activities because of their skewed distributions. The 2 randomized trials (psychiatrist- or psychologist-collaboration interventions) were then compared to assess any differences in the variables hypothesized to be related to relapse: demographics, intervention vs control status, history of major depressive episodes or chronic mood symptoms, age at onset of first episode, severity of depression (SCL, IDS), panic, neuroticism, disability, and coexisting medical conditions (Chronic Disease Score). As there was no significant difference between the 2 randomized trials in these key variables and both studies yielded similar intervention effects and relapse rates, samples from the 2 randomized trials were combined for analyses. Separate analyses were performed for baseline and 7-month variables.

Predictors of relapse were identified by means of forward stepwise logistic regression. Variables were selected for the regression analyses if they were hypothesized to be potential risk factors, had been identified by previous research, or yielded significant differences in bivariate comparisons of our sample. Five key covariates were included in all models: sex, age, study group (psychiatrist- or psychologist-collaboration), intervention status, and Chronic Disease Score. Whereas sex, age, intervention status, and Chronic Disease Score were hypothesized to be related to relapse, study group (psychiatrist- or psychologist-collaboration) was not. In the first step, education and marital status were allowed to enter the equation in a stepwise manner if they were statistically significant. In the second step, 8 baseline psychiatric and disability variables (age at onset of major depression, $\geq$2 previous episodes of depression or chronic mood symptoms for at least 2 years, generalized anxiety disorder or panic disorder, major depression, IDS and SCL scores, NEO score, and number of days with limited activity) were allowed to enter the model if they contributed significantly beyond the variables already present in the model. In the third step, the 7-month psychiatric and disability variables (IDS and SCL scores, and number of days with limited activity) were allowed to enter the equation in a stepwise manner. The final model retained only the 5 key covariates and variables that were significant at the .05 level. Odds ratios and their confidence intervals were calculated for the significant predictors. On the basis of the significant predictors from the logistic regression, risk factors were identified for relapse of depression. The number of risk factors for each patient was calculated. Analyses by χ^2 determined the relationship between rate of relapse and number of risk factors.

condition and adhere to long-term pharmacotherapy that may be associated with undesirable side effects.[14] The cost of maintenance pharmacotherapy and follow-up for this common disorder is also a significant consideration for patients as well as the health care system. The described recommendations for long-term pharmacotherapy to prevent relapse of depression have been based on efficacy trials in specialty settings.[15-17] Studies of the relapse rates, risk factors for relapse, and efficacy of maintenance pharmacotherapy have been conducted mainly in tertiary psychiatric populations. Since patients with major depression treated in the primary care setting have been found to have less severe depression, less psychiatric comorbidity, and better prognosis than those treated in specialty mental health clinics,[18,19] the relevance of these previous studies to primary care practices is uncertain.



Sample selection.

Table 1. Characteristics of Relapsed vs Nonrelapsed Depressed Patients

Patient Characteristics	Relapsed	No Relapse
Sample size, No. (%)	93 (37.1)	158 (62.9)
Female, No. (%)	72 (77.4)	123 (77.8)
Married, No. (%)	52 (55.9)	80 (50.6)
College graduates, No. (%)	79 (84.9)	120 (76.4)
Randomized to intervention group, No. (%)	49 (52.7)	85 (53.8)
Psychiatrist- (vs psychologist-) collaboration study, No. (%)	55 (59.1)	96 (60.8)
Age, mean ± SD, y	45.5 ± 13.6	48.8 ± 14.3
Age at onset of major depression, mean ± SD, y*	26.3 ± 16.7	33.5 ± 19.0
Chronic Disease Score, mean ± SD	1.45 ± 2.24	1.63 ± 2.48

*P<.01.

Since there are no empirical data on relapse based on patients in primary care settings, key questions remain. What is the rate of relapse of depression among primary care patients? Do previously identified risk factors predict relapse in primary care populations? Can recommendations based on evidence from specialty psychiatric settings be applied to primary care patients with similar outcomes? This information is necessary to design clinical programs aimed at relapse prevention among primary care patients. This report represents the first study, to our knowledge, on relapse of depression among primary care patients. We use 19-month follow-up data from patients enrolled in 2 randomized trials of a collaborative care program in a primary care setting.[9,20] The collaborative care interventions resulted in improved patient outcomes after acute- and continuation-phase treatment and provided an opportunity for a 1-year naturalistic follow-up study. The aims of this article are (1) to determine the rate of relapse of depression in primary care patients in the year after acute- and continuation-phase treatment and (2) to identify clinical predictors of relapse.

RESULTS

SAMPLE CHARACTERISTICS

The study cohort included 251 patients (Figure). The mean (± SD) age of this sample was 47.6 (± 14.1) years. Three quarters (76.8%) were women, 52.6% were married, 79.6% had received 1 or more years of college education, and a majority were employed (68.0%). At randomization, 40.2% (n = 101) had major depression and 59.8% (n = 150) had minor depression (2-4 *DSM-III-R* symptoms). The mean SCL score was 38.8 (± 11.8), and the mean IDS was 34.9 (± 13.0). Two or more previous episodes of major depression or chronic depressive symptoms were reported by 68.7% of patients. In the original collaborative care studies, patients enrolled in the study did not differ from patients who refused, in sex, mean age, or mean Chronic Disease Score. The original sample has been fully described in earlier reports.[9,20] Furthermore, there were no significant differences at baseline between those who completed the follow-up interviews and the original randomized group in sex, mean age, percentage who received the intervention, percentage with major depression, or SCL or IDS scores. There was also no significant difference in the proportion of intervention patients vs controls who missed at least 1 follow-up.

RELAPSE RATES AND USE OF HEALTH CARE SERVICES

Among the 251 patients, 37.1% (n = 93) either reported the return of symptoms in the previous year or were experiencing a major depressive episode at the 19-month assessment. Nine (9.7%) of those who relapsed (or 3.6% of the entire sample) met criteria for major depression at the 19-month interview. The relapse rates were similar for both acute-phase intervention trials (psychiatrist-collaboration study, 36.4%; psychologist-collaboration study, 38.0%). Intervention patients did not differ from control patients in the rate of relapse (36.3% vs 37.6%, respectively). Thus, we were able to pool the 2 study samples and their respective intervention and control groups into 1 combined sample. Of patients who reported relapse of depression, 72.8% also sought care for the symptoms. Patients who relapsed between 7 and 19 months made more primary care visits for depression in this 12-month period (median, 1 visit; range, 0-34 visits) than did patients with no relapse (median, 0 visits; range, 0-6 visits; $\chi^2_1 = 9.62$, $P = .002$).

CHARACTERISTICS OF THE RELAPSE GROUP (BIVARIATE ANALYSES)

Table 1 presents the characteristics of the relapse group. Patients who relapsed had their first episode of depression at a younger age than those who did not relapse (mean age, 26.3 vs 33.5 years, respectively; $t_{249} = 3.04$, $P = .003$). Demographic characteristics were similar in the 2 groups, with no significant differences in sex, age, marital status, education, intervention group status, or Chronic Disease Score.

As shown in **Table 2**, baseline clinical characteristics associated with relapse were history of at least 2 episodes of major depression or chronic mood symptoms for 2 years or longer ($\chi^2_1 = 5.06$; $P = .03$), a history of panic or generalized anxiety disorder ($\chi^2_1 = 5.79$;

Table 2. Baseline Psychiatric and Disability Characteristics of Relapsed vs Nonrelapsed Depressed Patients*

Baseline Psychiatric and Disability Status	Relapsed (n = 93)	No Relapse (n = 158)
≥2 Previous episodes of depression or chronic mood symptoms, No. (%)†	70 (75.3)	102 (64.6)
Generalized anxiety disorder or panic disorder, No. (%)†	57 (61.3)	72 (45.6)
Baseline major depression, No. (%)	42 (45.2)	59 (37.3)
IDS score, mean ± SD	36.5 ± 12.4	34.1 ± 13.2
SCL score, mean ± SD†	41.2 ± 11.3	37.5 ± 12.0
NEO Neuroticism Scale score, mean ± SD	16.7 ± 5.9	15.5 ± 5.7
Days with limited activity, median (range)	5 (0-90)	3 (0-90)

**IDS indicates Inventory of Depressive Symptoms; SCL, Hopkins Symptom Checklist.*
†P≤.05.

Table 3. Seven-Month Psychiatric and Disability Characteristics of Relapsed vs Nonrelapsed Depressed Patients*

Psychiatric and Disability Status at 7 mo	Relapsed (n = 93)	No Relapse (n = 158)
2-4 *DSM-III-R* symptoms, No. (%)†	39 (41.9)	41 (25.9)
SCL score, mean ± SD‡	18.7 ± 12.0	12.8 ± 10.2
IDS score, mean ± SD‡	17.6 ± 11.0	12.2 ± 9.5
Days with limited activity, mean ± SD§	7.92 ± 18.4	6.26 ± 15.8

*DSM-III-R *indicates* Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition; *SCL, Hopkins Symptom Checklist; and IDS, Inventory of Depressive Symptoms.*
†P≤.08.
‡P≤.001.
§P≤.008.

$P = .02$), and increased SCL score ($t_{249} = 2.44$; $P = .02$). Patients who relapsed were not more disabled at baseline as measured by activity limitation days because of illness compared with patients with no relapse ($\chi^2_1 = 0.92$; $P = .34$).

Table 3 presents characteristics of the relapse and nonrelapsing groups at the 7-month assessment. The relapse group had persistence of more depressive symptoms than the nonrelapsing group, as measured by increased SCL ($t_{249} = -4.21$; $P < .001$) and IDS scores ($t_{249} = -4.10$; $P < .001$). Among patients who relapsed, 41.8% had 2 to 4 *DSM-III-R* depressive symptoms (ie, met criteria for minor depression) compared with 25.6% of nonrelapsers ($\chi^2_2 = 7.06$; $P = .03$). Therefore, subthreshold symptoms were significantly more common in the relapse group. The number of days with limited activity, at 7 months, was also significantly related to relapse ($\chi^2_1 = 6.92$; $P = .008$)

PREDICTORS OF RELAPSE (LOGISTIC REGRESSION)

Logistic regression analyses controlled for sex, age, Chronic Disease Score, study group (psychiatrist- or psychologist-collaboration study), and intervention or control status. There were 2 significant predictors of relapse: (1) persistence of depressive symptoms (SCL score >13) at 7 months ($\beta = 1.20$; Wald $t = 15.92$; odds ratio, 3.33; confidence interval, 2.74-3.39; $P \leq .01$) and (2) history of at least 2 episodes of major depression or chronic mood symptoms for 2 years ($\beta = .74$; Wald $t = 4.59$; odds ratio, 2.09; confidence interval, 1.41-2.76; $P \leq .05$). There were no significant differences between groups on age; sex; Chronic Disease Score; intervention or control status; study group (psychiatrist- or psychologist-collaboration study); education; marital status; age at first onset of major depression; generalized anxiety disorder; panic disorder; baseline IDS, SCL, or NEO scores; or days with limited activity.

RISK FACTORS ASSOCIATED WITH RATE OF RELAPSE

On the basis of the final logistic model, we used these 2 risk factors to calculate a risk index for relapse. The estimated probability of relapse for different risk levels was as follows: no risk factors, 17.9%; 1 risk factor, 31.6%; and 2 risk factors, 56.6% (representing nearly a 3-fold increase in risk relative to no risk factors). The association between rate of relapse and number of risk factors was significant ($\chi^2_2 = 20.2$; $P = .001$).

COMMENT

This study represents the first investigation, to our knowledge, on relapse of depression in a primary care population. We found that the relapse rate of depression was substantial (37.1%) in the year after acute- and continuation-phase treatment for depression. The 2 predictors of relapse were (1) persistence of subthreshold depressive symptoms 7 months after initiation of pharmacotherapy and (2) history of at least 2 major episodes of depression or chronic mood disorders for 2 years or longer. Moreover, the likelihood of relapse in the following year was 31.6% for patients with 1 of these risk factors and 56.5% for patients with both. Bivariate analyses showed that other clinical characteristics associated with relapse were younger age at first episode of depression, presence of comorbid panic disorder or generalized anxiety disorder, and increased disability at the baseline interview. Other clinical features, such as coexisting chronic physical disorders, Neuroticism Scale score, number of pain symptoms, and demographic characteristics, were not associated with relapse of depression.

There are several limitations of this study. Results showing that patients' history of 2 or more episodes of major depression or a history of chronic depressive symptoms predisposes a patient to relapse need to be interpreted with some caution. Ideally, it would have been preferable to measure the variables separately. However, substantial missing data necessitated combining these 2 highly correlated measures. Although there was a 30% loss to follow-up during the 19-month study period, patients included in the sample were similar at baseline to patients who dropped out subsequently. The predictors of relapse were evaluated with a stepwise regression model. Replication of predictive models developed with a step-

wise variable selection often finds lower predictive power than estimated initially. For this reason, replication of the predictive analyses reported herein will be needed in future studies.

Selecting patients who were recognized as depressed by their physicians and willing to consider antidepressant treatment is both a strength and a limitation of this study. These results may not be generalized to depressed patients not seeking help in the primary care setting, those not recognized as depressed by their physicians, or those unwilling to consider pharmacotherapy. However, this selection process can enhance the generalizability of this effectiveness study to usual practice found in the general health care setting.

The *DSM-III-R*[23] diagnostic criteria were assessed at 19 months to diagnose major depression but could not be used to measure interval relapse in the 1-year follow-up period. Instead, questions regarding depression relapse adapted from the Diagnostic Interview Schedule[24] were used. Relapse was determined by retrospective report of symptoms in the preceding 1-year period. We are concerned with both potential overreporting and underreporting. Patients may have not remembered an episode of major depression that was short-lived and resolved before the 19-month follow-up. Conversely, some patients may have had minor depressive episodes misclassified as major. Ways to address this bias in future studies would be to plan more frequent assessments, to use a diagnostic instrument such as the Longitudinal Interval Follow-up Evaluation,[32] to have patients keep a diary of symptoms, or to interview significant others. However, more frequent interviews or journal entries could yield significant intervention effects. A comparison of the help-seeking behavior of the relapse group vs the nonrelapse group helped validate our study questions on depression relapse. As reported in the "Results" section, 72.8% of patients who reported relapse said they sought care for these symptoms. This suggests that the depressive symptoms were severe enough to prompt help-seeking for most patients in the relapse group. Furthermore, patients who suffered depression relapse made more visits to primary care physicians than patients who reported no relapse.

The finding that a small percentage of patients (1.9% and 3.6%) were experiencing major depression at 7 and 19 months, respectively, merits comment. Given the substantial relapse rates (37.1%), this finding suggests that the course of depression among primary care patients in this managed care population was often characterized by brief, recurrent episodes. In a previous study of predictors of persistence of depression in a similar GHC primary care population, only 15% of patients with major depression who were diagnosed as depressed by their primary care physicians still met criteria for this affective illness at the 4-month follow-up.[29] Other researchers have reported more chronicity of major depression in primary care samples with lower socioeconomic status and more coexisting chronic medical illness than the GHC population.[33]

Our data support Agency for Health Care Policy and Research recommendations that patients with a history of at least 2 episodes of major depression or chronic mood symptoms are at higher risk of relapse and are candidates for maintenance pharmacotherapy.[7] The primary care physician needs to ascertain this history in all depressed patients to better identify patients who would benefit from maintenance pharmacotherapy.

There are significant clinical implications for the finding that patients with subthreshold[2-4] depressive symptoms 7 months after initiating antidepressant therapy are at increased risk of relapse. When a patient improves and no longer meets *DSM-III-R* criteria for major depression but subthreshold symptoms persist, he or she still needs to be closely monitored by the primary care physician beyond acute-phase treatment to ensure symptom resolution and no return of depression. Monitoring of patient outcomes needs to be integrated into the primary care delivery system. Primary care providers may need to actively initiate assessment of patient progress and not simply rely on patient-initiated contacts. A patient's depressive symptoms such as fatigue, hopelessness, and psychomotor retardation can deter help-seeking. Other investigations have also shown that patients with persistent subthreshold symptoms are more likely to suffer relapse.[34-36]

To make these findings as clinically useful as possible, a risk factor index was developed. This index suggests that the presence of 2 coexisting risk factors rather than either risk factor alone is more important in identifying the high-risk patients. These 2 risk factors—persistent depressive symptoms and history of 2 or more previous episodes of depression or chronic mood symptoms—must be ascertained routinely in the management of depression. These high-risk patients need additional education on relapse prevention, such as how to recognize their individual early warning symptoms of depression, specific behaviors to boost medication adherence, and psychoeducational techniques to improve adaptation to acute and chronic stressors.

Although there is good evidence that patients in primary care settings have less severe depression and better prognosis than their tertiary care counterparts, it is noteworthy that the risk of relapse in this primary care population who are recognized as depressed by their physicians approaches those in specialty settings.[1,4,13] In view of the well-established evidence that the majority of depressed patients seek care from primary care providers,[10] this substantial rate of relapse in primary care underscores the significance of preventing depression relapse as an important public health issue.

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Reprints: Elizabeth H. B. Lin, MD, MPH, Center for Health Studies, Group Health Cooperative of Puget Sound, Met Park II, 1730 Minor Ave, Suite 1600, Seattle, WA 98101-1448.

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Clinical Pearl

Upper Extremity Deep Venous Thrombosis

In this series of 27 patients with upper extremity deep venous thrombosis, 8 (36%) of the 22 patients who underwent objective testing had a documented pulmonary embolism. (*Arch Intern Med*. 1997;157:57-62.)