The Undertreatment of Dysthymia

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Background: Dysthymia is a chronic depressive condition that is quite prevalent. This condition can exact a significant toll on the general health and quality of life in the affected individual. Despite the frequency and consequences of dysthymia, however, the condition is often not diagnosed or treated. We present data on prior treatment from 410 patients with DSM-III-R dysthymia, primary type, early onset without concurrent major depression.

Method: Axis I and II diagnoses were made by using the Structured Clinical Interviews for DSM-III-R, Patient Version (SCID-P) and SCID II for Personality Disorders. The Hamilton Rating Scale for Depression and the Clinical Global Impressions scale were also completed. Prior treatment was assessed, with special attention paid to previous antidepressant drug therapy and psychotherapy.

Results: Although the mean duration of dysthymia was about 30 years and almost half of the patients had previous episodes of major depression, only 41.3% had been treated with antidepressants and 56.1% with psychotherapy. A past history of major depression increased the frequency of prior antidepressant pharmacotherapy (45.7%) and psychotherapy (59.4%) compared with no history of major depression (36.8% and 40.9%, respectively). Comorbid personality disorder increased the likelihood of prior psychotherapy (70.7% vs. 49.6%) while having no effect on past pharmacotherapy. A history of substance abuse did not affect the history of antidepressant or psychotherapy treatment. In this study, dysthymia and psychosocial outcomes improved with sertraline and imipramine treatment.

Conclusion: Dysthymic patients in this sample were significantly undertreated. Newer antidepressant agents may alter the potential for pharmacotherapy interventions in this vulnerable population.

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Dysthymia, a chronic, mild-to-moderate depressive disorder lasting more than 2 years, was included in 1980 in the Third Edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III).[1] Studies indicate that this condition is prevalent, with estimates of its prevalence ranging from 3%[2] to 6%[3] in the general population, almost 7.0% in primary medical care settings,[4] and up to 36% in psychiatric outpatient clinics.[5]

Despite the high prevalence of this condition, dysthymia is infrequently diagnosed and even less commonly treated with pharmacotherapeutic agents. One study of psychiatric outpatients who met the DSM-III criteria for dysthymia found that a clinical diagnosis of dysthymia had been considered in less than half (13 [43%] of 30 cases).[5] Similarly, only 14 (41%) of 34 patients had received treatment with adequate levels of antidepressant medication, often after extended periods of treatment with psychotherapy alone or with other drugs such as benzodiazepines or antipsychotics.[5] The results from this study were echoed by an analysis of depression in medical outpatients, in which only 12 (43%) of 28 patients with a diagnosis of dysthymia by the Diagnostic Interview Schedule were recognized by their clinicians as having depression.[6] Of these 12 patients, antidepressants were prescribed for only 2 (17%). It is also important to note

that all forms of depression have been found to be underdiagnosed and undertreated, even obviously symptomatic forms of major depression.[7]

Even dysthymic patients who are given antidepressants may not be receiving adequate levels of treatment. Pharmacotherapeutic agents used to treat dysthymia are often prescribed at an inadequate dose or for an insufficient length of time because of the perception that the disorder is relatively mild. Moreover, many clinicians view chronic depression as a symptom of an underlying personality disorder warranting psychotherapeutic management rather than pharmacotherapy.[8]

The lack of recognition and treatment of dysthymia may have significant consequences, since approximately 17% of patients with dysthymia make serious suicide attempts.[9] In addition, dysthymic patients are at increased risk for major depressive disorder and poor health, and are more frequent users of medical services than the general population.[2,4] Results from the Medical Outcomes Study suggest that patients with dysthymia (with or without major depression) had significantly worse functional status and well-being than patients with depressive symptoms alone.[10]

Antidepressants are effective in the treatment of dysthymic patients with concurrent major depression ("double depression") and of those with dysthymia alone ("pure dysthymia").[8–12] Side effects of many antidepressant medications, however, pose a major problem in the treatment of dysthymia.

Although the serotonin selective reuptake inhibitors (SSRIs) are generally associated with fewer side effects than older classes of antidepressants, there have been few controlled studies in which these agents have been used to treat patients with dysthymia. Preliminary results from a multicenter double-blind trial of patients with dysthymia and concurrent major depression ("double depression") found that the efficacy of sertraline was similar to that of imipramine in the first 95 patients who completed the trial,[13] while a small (N = 32) trial of fluoxetine indicated that this agent was superior to placebo in the treatment of pure dysthymia.[14]

This paper will focus on demographic, diagnostic, and prior treatment data obtained from a multicenter, double-blind, placebo-controlled trial comparing the efficacy and safety of sertraline, imipramine, and placebo in the treatment of over 400 patients with early-onset primary dysthymia without concurrent major depression (pure dysthymia).[15,16] We hypothesized that dysthymia will have been relatively undertreated in the population. Further, we expected that comorbid conditions (like personality disorder or prior major depression) will have influenced the likelihood of previous treatment.

METHOD

These data were collected as part of a clinical trial of sertraline, imipramine, and placebo in the treatment of outpatients with dysthymia at 17 university-affiliated study sites. Written informed consent was obtained from all subjects. All patients were required to meet the following inclusion criteria: (1) an age of 25 to 65 years; (2) a DSM-III-R diagnosis of dysthymia, primary type, early onset; (3) a duration of dysthymia greater than 5 years, during which there was no period of more than 2 months in which the patient was free of depression symptoms; and (4) a total score of 12 or higher on the 29-item Hamilton Rating Scale for Depression (HAM-D).[17] Significant exclusion criteria included concurrent major depressive disorder, bipolar disorder, presence or history of psychosis, a primary diagnosis of panic disorder or generalized anxiety disorder, or a history of drug or alcohol dependency or abuse active within the last 6 months; serious suicidal risk; and failure to respond to adequate trials of two or more antidepressants or an adequate trial of imipramine (at least 4 weeks of treatment with at least 150 mg taken for 2 weeks or longer). Significant medical conditions that could interfere with the patient's participation in the study excluded patients. Pregnant and lactating women were also excluded.

The methods and results of the primary treatment outcome study have been reported elsewhere.[15] In brief, eligible patients were placed on a single-blind placebo washout for 1 week, during which time baseline data were obtained. Axis I and II diagnoses were made by trained raters using the Structured Clinical Interview for DSM-III-R, Patient Version (SCID-P)[18] and SCID II for Personality Disorders.[19] Patients who had Clinical Global Impressions (CGI) improvement scores ≤ 2 or HAM-D scores < 12 at the end of placebo washout were excluded from further participation. The remainder were randomly assigned to 12 weeks of treatment with sertraline, imipramine, or placebo. Sertraline was initiated at 50 mg/day and titrated to a maximum dose of 200 mg/day, and imipramine treatment began with 50 mg/day and could be increased to a maximum of 300 mg/day. Titration was performed in the absence of dose-limiting side effects unless a therapeutic response had been achieved.

We collected extensive demographic and clinical information on each participant, including age, sex, race, age at onset of dysthymia, total duration of illness, duration of current dysthymic episode, and prior treatment, including whether subjects had received any previous antidepressant pharmacotherapy or psychotherapy. Specific types of drug treatment or psychotherapy and duration of treatment could not be obtained systematically because of the subjects' lack of information or problems with recall. Therefore, the quality and extent of treatment are unknown. Finally, we questioned subjects about family history of mental disorders.

The primary symptom and efficacy measure in the drug treatment study was the HAM-D (17- and 29-item). Efficacy was determined by total score and by change in

HAM-D total score from baseline as calculated by using week-by-week last observation carried forward (excluding baseline) (LOCF). Efficacy was also assessed by Clinical Global Impressions ratings of severity (CGI-S) and improvement (CGI-I). A number of additional measures were used as secondary indicators of efficacy, including the Social Adjustment Scale, self-rated version (SAS-SR),[20] the Montgomery-Asberg Depression Rating Scale (MADRS),[21] and the Inventory of Depressive Symptoms (IDS).[22,23]

Statistical Analysis

All clinical data were analyzed using the Statistical Analysis System (SAS) version 6.08 (SAS Institute, Cary, N.C.). Of the 416 persons who participated in the study, 412 received at least one dose of medication and were included in the analysis of safety and toleration data. Of this number, 410 had efficacy measurements at both baseline and at least one follow-up visit. This constituted the intent-to-treat sample that was evaluated for efficacy of treatments.[15]

Continuous data (e.g., age, duration of illness, applicable efficacy assessments) were compared with analysis of variance (ANOVA) models that included treatment-group and center main effects and the treatment-group × center interaction effects. Chi-square tests were computed, as appropriate, for demographic characteristics (e.g., prevalence of concomitant and previous medication usage, present concurrent medical conditions, and history of illness). Frequency distributions were prepared to characterize the patients with respect to age at entry into the study, age at the first depressive episode, the approximate history of the primary and secondary illnesses, duration of the current episode, and frequency of previous episodes.

An alpha level of .05 was assumed, and two-sided tests were performed throughout the efficacy analysis in order to declare significance for inferential statistics. The primary measures of efficacy for symptom assessments were the changes from baseline to endpoint, as defined by LOCF while the patient was taking double-blind medication. Analysis of covariance (ANCOVA) models, with baseline values serving as the covariates, were used as the omnibus tests of significance to evaluate the between-group and center main effects and the between-group × center interaction effects. Significant main effects were further explored by using unpaired t tests. The significance of the within-group changes from baseline was assessed with paired t tests. The significance of the between-group differences in responder and remitter rates (i.e., defined with respect to HAM-D, CGI-I, and criteria for dysthymia) was determined with chi-square tests.

Other continuous data were analyzed by Student's t tests, while dichotomous data (including presence or absence of prior treatments) were evaluated by the Cochran-Mantel-Haenszel statistic as appropriate.

Table 1. Demographic and Diagnostic Data in 410 Dysthymic Patients

Variable	Value
Female sex, N (%)	266 (64.9)
Age (y), mean ± SD	41.7 ± 9.1
Race, N (%)	
White	390 (95.1)
Black	9 (2.2)
Asian	2 (0.5)
Other	9 (2.2)
Duration of illness (y), mean ± SD	29.4 ± 10.6
Age at onset (y), mean ± SD	12.1 ± 4.8
Duration of current dysthymic episode (y), mean ± SD	29.4 ± 10.6
Prior history of major depression, N (%)	208 (50.7)
Number of lifetime episodes of major depression, N (%)	
None	202 (49.3)
One	92 (22.4)
Two or more	116 (28.3)

RESULTS

Study Participants

A total of 416 outpatients were randomly assigned to treatment in one of the three study arms. Of these, 4 were discontinued from the study prior to taking study medication and 2 took study medications but failed to make their subsequent follow-up visits after baseline. Therefore, 410 patients had baseline and at least one follow-up visit assessment.

Table 1 presents demographic and diagnostic data for the patients studied. Only 42.9% were currently married, and 29.3% had never married. Patients were generally well educated. Almost 30% of the patients had graduate school or professional training (N = 121), while an additional 109 patients (26.6%) had graduated from college. Partial college training had been obtained by 114 patients (27.8%), and 55 patients (13.4%) ended their education after graduating from high school. Only 11 of the patients (2.7%) had failed to complete high school. Despite the high level of education achieved, 87 patients (21.2%) were unemployed. While 274 (66.8%) were employed in their chosen occupation, 22 (5.4%) were engaged in other work, 10 (2.4%) were retired, and 16 (3.9%) were students.

There were no significant differences among the three randomization groups in terms of sex, mean age, race, marital or employment status, education level, mean duration of dysthymia, or age at onset of dysthymia. Each study participant met DSM-III-R criteria for primary dysthymia, early onset, as determined by the SCID-P.

Patients were, in general, mildly depressed at study entry as indicated by a mean ± SD HAM-D 17-item baseline score of 13 ± 3.9 (range, 12.7–13.4) and a mean baseline HAM-D 29-item score of 21.

Comorbidity and Family History

The lifetime prevalence of Axis I psychiatric disorders (> 3%) in the 410 patients enrolled in the dysthymia study

Table 2. Lifetime Prevalence of Axis I Diagnoses (> 3%) in 410 Dysthymic Patients

Diagnosis	N	%
Major depression	208	50.7
Substance abuse	108	26.3
Panic disorder/agoraphobia without a history of panic	35	8.6
Social phobia	42	10.2
Eating disorders (anorexia/bulimia nervosa)	17	4.1

Table 3. Lifetime Prevalence of Axis II Cluster Diagnoses and Personality Disorders in 410 Dysthymic Patients

	Sertraline (N = 134)		Imipramine (N = 136)		Placebo (N = 140)	
Diagnosis	N	%	N	%	N	%
Cluster diagnoses[a]						
A	11	8.2	12	8.8	21	15.0
B	13	9.7	17	12.5	18	12.9
C	63	47.0	61	44.9	69	49.3
Personality disorders						
None	60	44.8	60	44.1	55	39.3
One	40	29.9	42	30.9	48	34.3
Two or more	34	25.4	34	25.0	37	26.4

[a]Cluster A = paranoid, schizotypal, and schizoid disorders; Cluster B = antisocial, borderline, histrionic, and narcissistic disorders; Cluster C = avoidant, dependent, self-defeating, obsessive-compulsive, and passive-aggressive disorders.

is shown in Table 2, and the lifetime prevalence of Axis II cluster diagnoses and personality disorders is presented in Table 3. The most common lifetime Axis I comorbid disorder was prior major depression, which was reported by 50.7% of the patients. Lifetime prevalence of alcohol and substance abuse, a category that encompassed abuse of or dependency on alcohol or substances such as cannabis, sedatives, stimulants, opioids, cocaine, or hallucinogens, also was common, involving 26.3% of the patients. Alcohol was the most common substance abused, with over 20% of the patients reporting alcohol abuse or dependency. The Axis II diagnoses most commonly found were DSM-III-R Cluster C disorders including avoidant (N = 101, 24.6%), obsessive-compulsive (N = 96, 23.4%), self-defeating (N = 45, 11.0%), passive-aggressive (N = 35, 8.5%), and dependent (N = 34, 8.3%) personality disorders.

During patient interviews at baseline, more than half of the patients reported a family history of affective disorder in first-degree relatives (233 [56.8%] of 410) and 120 patients (29.3%) reported the occurrence of an affective disorder in second-degree relatives. A family history of alcohol and drug abuse was almost as common, with 160 patients (39.0%) reporting first-lineal and 103 (25.1%) reporting second-lineal cases of substance abuse.

Previous Treatment

The mean ± SD duration of dysthymia prior to enrollment in this study was approximately 29.4 ± 10.6 years

Table 4. Prior Treatment of Patients With Dysthymia

	Previous Treatment[a]			
	Antidepressant		Psychotherapy	
Patient History	N	%	N	%
All patients (N = 410)	169/409	41.3	201/358	56.1
History of major depression				
Yes (N = 208)	95/208[b]	45.7	129/182[c]	70.9
No (N = 202)	74/201	36.8	72/176	40.9
Comorbid personality disorder				
Yes (N = 279)	148/279	53.0	142/239[d]	59.4
No (N = 130)	68/130	52.3	59/119	49.6
History of substance abuse				
Yes (N = 108)	58/108	53.7	55/98	56.1
No (N = 302)	158/301	52.5	146/260	56.2

[a]Denominators of ratios indicate available data (total minus missing).
[b]Previous antidepressant treatment by history of major depression: Cochran-Mantel-Haenszel value = 3.46, df = 1, p < .07.
[c]Previous psychotherapy by history of major depression: Cochran-Mantel-Haenszel value = 28.53, df = 1, p < .0001.
[d]Previous psychotherapy by comorbid personality disorder: Cochran-Mantel-Haenszel value = 3.12, df = 1, p < .08.

with a minimum duration of 8 years and a maximum of 62 years. Only 41.2% of 410 patients randomly assigned to the 12-week study had received any prior treatment with antidepressant medication, while 56.1% had received some form of psychotherapy (Table 4). Slightly more than half (50.7%) of the subjects reported a history of major depression. Of this group, 45.7% had a history of antidepressant pharmacotherapy. In contrast, 36.8% of subjects without a history of major depression had been treated with antidepressants, which represents a statistical trend (Cochran-Mantel-Haenszel value = 3.46, df = 1, p < .07). Persons with a history of major depression were much more likely to have received psychotherapy (70.9%) versus those without such a history (40.9%) (Cochran-Mantel-Haenszel value = 28.53, df = 1, p < .0001).

Of the patients who had a previous episode of major depression and had been treated with antidepressants, 36 (37.9%) of 95 reported that they were much improved, 23 (24.2%) reported minimal improvement, and 36 (37.9%) reported no change or that they felt worse following prior antidepressant treatment.

Thirty-four (26.4%) of the 129 patients who had previous major depression and were treated with psychotherapy reported that they were much improved after psychotherapy. Seventy patients (54.3%) reported minimal improvement after psychotherapy, and 25 (19.4%) reported that they had no change.

Electroconvulsive therapy (ECT) had been administered to 3 of the patients with prior major depression. All 3 patients categorized their response as much improved after ECT.

Prior history of substance abuse had no effect on whether participants had received previous treatment with antidepressants or psychotherapy. Comorbid personality disorder did not change the frequency of prior treatment

with antidepressants. However, there was a trend toward a significant difference in frequency of past psychotherapy between persons with a comorbid personality disorder (59.4%) versus those without (49.6%) (Cochran-Mantel-Haenszel value = 3.12, df = 1, $p < .08$).

Efficacy and Adverse Effects of Sertraline and Imipramine Treatment

Efficacy and safety data from this study have been previously reported[15,16] and are briefly summarized here. The response (defined as a CGI improvement score of 1 or 2 [very much or much improved]) and full remission (defined as no longer meeting DSM-III-R criteria for dysthymia *and* a score of 0 on HAM-D Item 1 [depressed mood]) rates were similar for both active treatment groups and were significantly higher for both sertraline and imipramine compared with placebo. Both drugs produced a significantly greater mean decrease in 17-item HAM-D, MADRS, and total IDS scores from baseline to endpoint than placebo, and the two active treatments did not differ significantly.[15] Psychosocial outcomes improved significantly with antidepressant treatment.[16]

The proportion of completing patients in both the sertraline and placebo groups was significantly greater than that in the imipramine group. The dropout rate due to side effects in the sertraline group was only slightly higher than the dropout rate in the placebo group and less than one third the dropout rate due to side effects reported in the imipramine group.

DISCUSSION

The data obtained from this study support previous results that dysthymia is undertreated.[5,24] The patients enrolled in this clinical trial had dysthymia, primary type, early onset with a mean duration of approximately 30 years, and almost half of them had also received a lifetime diagnosis of major depression. However, only 56% had received psychotherapy and 41% treatment with antidepressant medication at any time during their illness. These findings are consistent with those of studies of major depressive disorder, which have shown rates of undertreatment ranging from 78% to 53%.[25–27] Given the large number of persons affected with dysthymia, the high levels of psychiatric comorbidity, and the negative impact on health and quality of life, this undertreatment represents a significant public health and economic problem.

Comorbid disorders were common in this group of patients. More than half reported a history of major depression, while 26.3% had a past history of substance abuse disorder. Comorbid personality disorder was diagnosed in 68.2% of the group. The presence of substance abuse had no effect on the likelihood of prior treatment. Subjects with a history of major depression, however, were more likely to have received pharmacotherapy (46%) than those without this history (37%) at a trend level (two-tailed $p < .07$), and were statistically significantly more likely to have received psychotherapy (71% vs. 41%). In fact, subjects with "pure dysthymia" (i.e., dysthymic disorder without a history of major depression) had a remarkably low rate of prior treatment. Finally, those persons with personality disorder had higher rates of treatment with psychotherapy (59%) than those without (50%) at a trend level (two-tailed $p < .08$), with no differences in frequency of pharmacotherapy. Although specific information about the quality of prior pharmacotherapy is unknown in this sample, it is reasonable to assume that a sizable proportion of the pharmacotherapy-treated subjects had received inadequate therapy,[26] further reducing the impact of previous treatment. These data clearly support previous reports that persons with dysthymia are unlikely to receive appropriate therapeutic intervention.[5,24]

The undertreatment of dysthymia probably stems from several factors. One is clinicians' lack of recognition of mild depressive disorders, particularly mild chronic depression. Similarly, the chronicity of symptoms may reduce the likelihood that patients and families will recognize the depression, since depression often is perceived as the person's usual state. This may explain why patients generally do not seek treatment unless they are experiencing a current episode of major depression. Beyond the problem of underrecognition, however, is the perception that there are no effective pharmacotherapeutic options for dysthymia. Moreover, many mental health professionals think of dysthymia as a personality disorder that requires lengthy psychotherapy rather than as a pharmacologically treatable mood disorder. For example, in the present study, dysthymics were somewhat more likely to have received psychotherapy (56%) than pharmacotherapy (41%). Not surprisingly, comorbid personality disorder raised the chance for earlier psychotherapy considerably (71% vs. 50%). However, somewhat unexpectedly, a prior history of major depression among dysthymics increased the likelihood of prior psychotherapy (71%) more than of prior pharmacotherapy (a low 46%). This high frequency of prior psychotherapy relative to pharmacotherapy is especially troublesome given the fact that few (26%) double depressives reported significant improvement with psychotherapy, in contrast to the generally positive results with pharmacotherapy in the current project. The preference for psychotherapy compared with pharmacotherapy may have resulted, in part, from compliance problems with older antidepressants related to troublesome adverse effects.

There are, of course, limitations affecting our research. Our project represents a multicenter study conducted in university-affiliated medical centers, which may have introduced unintended selection biases into the study group. For example, the study group overall had a higher than expected level of education. On the other hand, relatively

higher educational attainment and self-selection into an academic medical setting are likely to have increased prior experience of treatment, rather than to have decreased it. The exclusion of patients who had previously failed an adequate trial of treatment with imipramine may have resulted in the removal of certain persons with prior treatment from the sample, but this is unlikely to have had a major effect. Of the patients screened over the phone prior to study entry regarding previous antidepressant use, very few were excluded on this basis. Many dysthymic patients treated with imipramine in the past could be expected to have received inadequate dose or duration of treatment. Further, this study and earlier trials[12,13] indicate that imipramine, used adequately, is an effective treatment for dysthymia. Therefore, it is doubtful that a significant number of subjects were excluded on this basis. It is similarly improbable that substantial numbers of subjects were excluded on the basis of prior treatment failure with sertraline. At the time of the study initiation, sertraline had been marketed in the United States for less than 1 year. Finally, some of the information gathered in this study was of a retrospective nature and, therefore, could have been subject to negative retrospective bias in this depressed patient population. However, this is unlikely to have significantly biased important data such as whether prior treatment had been received. Although biases may have been introduced into the study group, it seems doubtful that they have nullified the basic conclusion of the study: dysthymia is seriously undertreated.

Appropriate treatment of dysthymia may result not only in disease remission, thus improving the quality of life of the individual, but also in an improved long-term prognosis. Because dysthymia is a risk factor for the development of major depressive episodes,[28,29] prompt treatment of patients with dysthymia may prevent the development of more severe affective conditions. Similarly, the lifetime prevalence of substance abuse (including alcohol) was high in this group of dysthymic patients, suggesting that untreated dysthymia may be a risk factor for development of substance abuse. The Epidemiologic Catchment Area study has reported the prevalence rate of substance abuse among dysthymics as 31.4% (a rate similar to that of 26.3% in the present study), while the prevalence of alcohol abuse alone was 20.9% (vs. 20% in this project).[30]

Undertreatment of dysthymia also may have a serious long-term impact on educational and occupational attainment. Kessler et al.[31] reported that persons with early-onset psychiatric disorders account for 14.2% of high school dropouts and 4.7% of college dropouts, with 1.9% and 0.3%, respectively, suffering specifically from mood disorders. The subjects in the current study had a relatively high level of educational achievement, but relatively high rates of unemployment (21%). This finding certainly may have been influenced by the fact that the study offered free treatment, but nonetheless suggests an adverse impact of dysthymia on work ability.

Our results indicate that dysthymia is significantly undertreated. This is especially lamentable given the demonstrated efficacy of sertraline and imipramine relative to placebo in the treatment of persons with dysthymia in this project. Sertraline was particularly well tolerated in this acute treatment study. Early discontinuation due to side effects was seen in only 6% of the sertraline-treated subjects compared with 18.4% of imipramine-treated subjects ($p < .0001$). Improved recognition of dysthymia as a treatable disorder and the availability of effective agents with favorable side effect profiles should result in a more vigorous therapeutic approach and better outcome for this disorder.

Drug names: fluoxetine (Prozac), imipramine (Tofranil and others), sertraline (Zoloft).

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third Edition. Washington, DC: American Psychiatric Association; 1980
2. Weissman MM, Leaf PJ, Bruce ML, et al. The epidemiology of dysthymia in five communities: rates, risks, comorbidity, and treatment. Am J Psychiatry 1988;145:815–819
3. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 1994;51:8–19
4. Howland RH. General health, health care utilization, and medical comorbidity in dysthymia. Int J Psychiatry Med 1993;23:211–237
5. Markowitz JC, Moran ME, Kocsis JH, et al. Prevalence and comorbidity of dysthymic disorder among psychiatric outpatients. J Affect Disord 1992;24:63–71
6. Pérez-Stable EJ, Miranda J, Muñoz RF, et al. Depression in medical outpatients: underrecognition and misdiagnosis. Arch Intern Med 1990;150: 1083–1088
7. Keller MB. Depression: underrecognition and undertreatment by psychiatrists and other health care professionals. Arch Intern Med 1990;150:946–948
8. Harrison WM, Stewart JW. Pharmacotherapy of dysthymic disorder. In: Kocsis JH, Lein DN, eds. Diagnosis and Treatment of Chronic Depression. New York, NY: Guilford Press; 1995:124–145
9. Howland RH. Pharmacotherapy of dysthymia: a review. J Clin Psychopharmacol 1991;11:83–92
10. Wells KB, Stewart A, Hays RD, et al. The functioning and well-being of depressed patients: results from the Medical Outcomes Study. JAMA 1989;262:914–919
11. Stewart JW, Quitkin FM, Klein DF. The pharmacotherapy of minor depression. Am J Psychother 1992;46:23–36
12. Kocsis JH, Sutton BM, Frances AJ. Long-term follow-up of chronic depression treated with imipramine. J Clin Psychiatry 1991;52:56–59
13. Keller MB, Harrison W, Fawcett JA, et al. Treatment of chronic depression with sertraline or imipramine: preliminary blinded response rates and high rates of undertreatment in the community. Psychopharmacol Bull 1995; 31(2):205–212
14. Hellerstein DJ, Yanowitch P, Rosenthal J, et al. A randomized double-blind study of fluoxetine versus placebo in the treatment of dysthymia. Am J Psychiatry 1993;150:1169–1175
15. Thase ME, Fava M, Halbreich U, et al. A placebo-controlled randomized clinical trial comparing sertraline and imipramine for the treatment of dysthymia. Arch Gen Psychiatry. In press
16. Kocsis JH, Davidson J, Zisook S, et al. Double-blind treatment comparison of sertraline, imipramine, and placebo in the treatment of dysthymia: psychosocial outcomes. Am J Psychiatry. In press
17. Hamilton M. Rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62
18. Spitzer RL, Williams JBW, Gibbon M. Instruction Manual for the Structured Clinical Interview for DSM-III-R (SCID, 4/1/87 revision). New York, NY: Biometric Research, New York State Psychiatric Institute; 1987

19. Spitzer RL, Williams JBW, Gibbon M. Structured Clinical Interview for DSM-III-R Personality Disorders (SCID-II, 10/15/86). New York, NY: Biometric Research, New York State Psychiatric Institute; 1986
20. Weissman MM, Bothwell S. Assessment of social adjustment by patient self-report. Arch Gen Psychiatry 1976;33:1111–1115
21. Montgomery SA, Asberg M. New depression rating scale designed to be sensitive to change. Br J Psychiatry 1979;134:382–389
22. Rush AJ, Giles DE, Schlesser MA, et al. The inventory for depressive symptomatology (IDS): preliminary findings. Psychiatry Res 1986;18: 65–87
23. Rush AJ, Hiser W, Giles DE. A comparison of self-reported versus clinician-rated symptoms in depression. J Clin Psychiatry 1987;48: 246–248
24. Keller MB. Dysthymia in clinical practice: course outcome and impact on the community. Acta Psychiatr Scand 1994;89(suppl 383):24–34
25. Brugha TS, Bebbington PK. The undertreatment of depression. Eur Arch Psychiatry Clin Neurosci 1992;242:103–108
26. Keller MB, Lavori PW, Klerman GL, et al. Low levels and lack of predictors of somatotherapy and psychotherapy received by depressed patients. Arch Gen Psychiatry 1986;43:458–466
27. Brugha TS. Depression undertreatment: lost cohorts, lost opportunities? Psychol Med 1995;25:3–6
28. Kovacs M, Feinberg TL, Crouse-Novak M, et al. Depressive disorders in childhood, II: a longitudinal study of the risk for a subsequent major depression. Arch Gen Psychiatry 1984;41:815–819
29. Keller MB, Lavori PW. Double depression, major depression, and dysthymia: distinct entities or different phases of a single disorder? Psychopharmacol Bull 1984;20:399–402
30. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. JAMA 1990;264:2511–2518
31. Kessler RC, Foster CL, Saunders WB, et al. Social consequences of psychiatric disorders, I: educational attainment. Am J Psychiatry 1995;152: 1026–1032