Article

Five-Year Course and Outcome of Dysthymic Disorder: A Prospective, Naturalistic Follow-Up Study

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Objective: There have been few naturalistic follow-up studies of dysthymic disorder. This study describes the 5-year course and outcome of dysthymic disorder.

Method: The authors conducted a prospective, longitudinal follow-up study of 86 outpatients with early-onset dysthymic disorder and 39 outpatients with episodic major depressive disorder. Follow-ups, conducted 30 and 60 months after entry into the study, rated patients on the Longitudinal Interval Follow-Up Evaluation and the Modified Hamilton Rating Scale for Depression.

Results: The estimated 5-year recovery rate from dysthymic disorder was 52.9%. Among patients who recovered, the estimated risk of relapse was 45.2% during a mean of 23 months of observation. Patients with dysthymic disorder spent approximately 70% of the follow-up period meeting the full criteria for a mood disorder. During the course of the follow-up the patients with dysthymic disorder exhibited significantly greater levels of symptoms and lower functioning and were significantly more likely to attempt suicide and to be hospitalized than were patients with episodic major depressive disorder. Finally, among patients with dysthymic disorder who had never experienced a major depressive episode before entry into the study, the estimated risk of having a first lifetime major depressive episode was 76.9%.

Conclusions: Dysthymic disorder is a chronic condition with a protracted course and a high risk of relapse. In addition, almost all patients with dysthymic disorder eventually develop superimposed major depressive episodes. Although patients with dysthymic disorder tend to show mild to moderate symptoms, from a longitudinal perspective, the condition is severe.

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Dysthymic disorder is a low-grade, chronic, depressive condition that is defined and distinguished from major depressive disorder primarily on the basis of course (1). Dysthymic disorder is common, affecting 3%–6% of individuals in the community (2, 3) and 22%–36% of outpatients in mental health settings (4, 5). However, given its high prevalence and the central role of chronicity in its definition, there are surprisingly few data on the naturalistic course of dysthymic disorder.

Of the few existing prospective longitudinal studies of dysthymic disorder, most have used small study groups and short (1–2 year) follow-up periods (6–12). These studies have indicated that approximately 40% of the individuals with dysthymic disorder recover within 24–30 months of study entry (6, 8, 9). It is not known whether the rate of recovery increases substantially with longer follow-ups. In addition, no data are available on the probability of relapse or recurrence among patients who have recovered from dysthymic disorder.

Compared to patients with episodic major depressive disorder, patients with dysthymic disorder are less severely depressed at initial examination but exhibit higher levels of symptoms in follow-ups conducted 6–30 months later (9, 13, 14). A small proportion of adults and children with dysthymic disorder develop bipolar disorder during the course of follow-up, although the risk may not differ from that of individuals with major depressive disorder (10, 15). Individuals with dysthymic disorder are at high risk of developing superimposed major depressive episodes (10, 16). Although there is a high probability of recovering from a superimposed major depressive episode, there is a substantial risk of relapsing into another episode (7–10, 14). Comparisons of the rates of recovery from, and relapse into, major depressive episodes between patients with dysthymic disorder and patients with episodic major depressive disorder have been inconsistent (7–10, 14).

For chronic conditions such as dysthymic disorder, short-term follow-ups are of limited value, because it takes a number of years to determine the probability of recovery and even longer to ascertain relapse or recurrence rates. We recently reported the results of a 30-month follow-up of a cohort of 86 outpatients with early-onset dysthymic disorder, contrasting them to a "near-neighbor" comparison group of 39 patients with episodic major depressive disorder (9). We focused on the early-onset (less than 21 years) subtype because it is the prototypical and most common form of dysthymic disorder (1, 13, 15). We have continued to follow this study group, and in this arti-

cle we report the major findings from our 5-year follow-up study. This article presents data regarding eight issues related to patients with dysthymic disorder: 1) the 5-year rate of recovery; 2) the rate of relapse among patients who had recovered; 3) the risk of developing bipolar disorder; 4) the risk of developing a first lifetime major depressive episode for patients with no prior history of major depressive disorder; 5) the rates of recovery from, and relapse into, superimposed major depressive episodes; 6) a comparison of course and outcome between patients with dysthymic disorder and patients with episodic major depressive disorder; 7) mortality and suicide attempts; and 8) the study group's naturalistic treatment experience. In future reports, we will describe the course of social adjustment and comorbid conditions in this study group and examine the impact of a broad range of clinical, psychosocial, familial, and treatment variables on the course of dysthymic disorder.

Method

Subjects

The study group and methods for the initial evaluation have been described previously (9, 17). The original study group included 97 outpatients with DSM-III-R primary early-onset dysthymic disorder and 45 outpatients with nonchronic major depressive disorder. Patients were between the ages of 18 and 60, spoke English, and had knowledge of at least one first-degree relative. Patients with episodic major depressive disorder were also required to have an onset before age 35. In addition, the major depressive disorder could not be due to another axis I disorder or chronic medical condition, and these patients could not have a past history of dysthymic disorder. Patients were selected from individuals consecutively admitted to the State University of New York at Stony Brook's Outpatient Psychiatry Department and Psychological Center. In addition, several patients were referred from a community mental health center and the State University of New York at Stony Brook's University Counseling Center.

At least one follow-up evaluation was completed for 86 of 97 (88.7%) of the patients with dysthymic disorder and 39 of 45 (86.7%) of the patients with episodic major depressive disorder. The mean interval of follow-up was 57.5 months (SD=7.5) for the patients with dysthymic disorder and 58.2 months (SD=6.4) for the patients with episodic major depressive disorder ($t=0.52$, $df=123$, $p=0.61$). Patients who were and were not available for follow-up were compared on the following baseline variables: age, sex, race, marital status, education, socioeconomic status (18), score on the Global Assessment of Functioning scale (19), score on the Modified Hamilton Rating Scale for Depression (20), concurrent anxiety disorder, lifetime history of substance abuse or dependence, comorbid personality disorder, age at onset of dysthymic disorder or major depressive disorder, and, as applicable, recurrent subtype of major depressive disorder. None of the comparisons within the dysthymic disorder group was significant. In the episodic major depressive disorder group, patients who had been followed up were significantly younger (mean=29.9, SD=7.7) than those patients who had not been followed up (mean=42.5, SD=11.2) ($t=3.51$, $df=43$, $p<0.001$) and had an earlier age at onset of major depressive disorder (mean=23.1, SD=6.0) than those patients without follow-ups (mean=30.0, SD=6.1) ($t=2.42$, $df=42$, $p<0.05$).

Because this was a naturalistic study, there was no attempt to control treatment. However, we obtained detailed information about treatment from the patients and their medical records. Treatment was coded by using 4-point scales for the adequacy of antidepressant medication and the frequency of psychotherapy (21). We did not code the quality or orientation of psychotherapy. For antidepressant medication, the following scale was used: 0=no medication, 1=medication failed to meet the criteria for a probably or definitely adequate dose, 2=dose met the criteria for probable adequacy, and 3=dose met the criteria for definite adequacy (22). For psychotherapy, the following scale was used: 0=no psychotherapy, 1=monthly sessions, 2=biweekly sessions, and 3=weekly sessions. None of the patients participated in other research protocols during the follow-up period. Written informed consent was obtained after the subjects received a complete description of the study.

Baseline Evaluation

A baseline evaluation was conducted shortly after the patients were admitted. It included the Structured Clinical Interview for DSM-III-R (19) and the 24-item modified Hamilton depression scale (20), which focused on the worst week of the patient's current major depressive episode or the worst week in the past month if there was no current major depressive episode. As reported elsewhere, the interrater reliability of our baseline diagnoses was good to excellent (23).

Follow-Up Evaluations

Follow-up evaluations were conducted 30 and 60 months after entry into the study. Follow-up assessments included the Longitudinal Interval Follow-Up Evaluation (24) and the 24-item modified Hamilton depression scale (20). The Longitudinal Interval Follow-Up Evaluation is a semistructured interview that assesses the course of axis I disorders and treatment throughout the follow-up period. Following conventions from the Longitudinal Interval Follow-Up Evaluation, we defined "recovery" as a period of at least 8 consecutive weeks with minimal or no symptoms and "relapse" as meeting the full criteria for a disorder after having recovered. Because individuals with dysthymic disorder occasionally experience temporary remissions of several months at some time in the course of their illness, we also employed an alternative, more conservative, definition of recovery from dysthymic disorder that required at least 26 consecutive weeks of minimal or no symptoms.

Although the Longitudinal Interval Follow-Up Evaluation was originally developed for follow-up periods of 6 months, it can be adapted for follow-ups of any length and has been used successfully for follow-ups of up to 12-year intervals (25). In this study, we used a version of the Longitudinal Interval Follow-Up Evaluation that had been modified by its authors to assess DSM-III-R criteria. To facilitate the recall and dating of episodes of psychopathology, we added a section to the beginning of the interview that elicited the occurrence and dates of major life changes and stressors during the follow-up period (2).

Follow-up interviews were conducted by a master's-level psychiatric social worker, a master's-level psychologist (S.R.), a doctoral-level clinical psychology research fellow, and three advanced graduate students in clinical psychology (including J.B.L.). All interviewers were blind to the original diagnoses of the subjects, and different interviewers conducted the baseline, 30-month, and 60-month evaluations for each patient.

To assess interrater reliability, one rater independently rated 13 audiotapes of several randomly selected interviews from the Longitudinal Interval Follow-Up Evaluation conducted by the other interviewers. Kappas were 0.83 for recovery from dysthymic disorder, 0.75 for recovery from a major depressive episode, and 0.68 for relapse into a major depressive episode. The intraclass correlation (26) for the modified Hamilton depression scale was 0.95.

TABLE 1. Baseline Characteristics of Patients With Dysthymic Disorder and Patients With Episodic Major Depressive Disorder

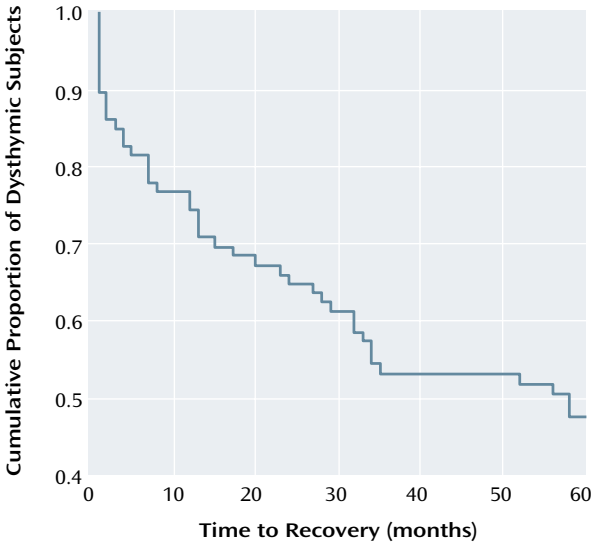
Characteristic	Dysthymic Disorder (N=86)		Episodic Major Depressive Disorder (N=39)	
	N	*%*	*N*	*%*
Male sex	21	24.4	14	35.9
White race	79	91.9	33	84.6
Marital status				
Single	40	46.5	18	46.2
Married	27	31.4	11	28.2
Separated/divorced	17	19.8	10	25.6
Widowed	2	2.3	0	0.0
Recurrent subtype of major depressive disorder[a]	39	78.0	23	59.0
Concurrent anxiety disorder	31	36.0	7	17.9[b]
Lifetime substance abuse or dependence	44	51.2	11	28.2[c]
Personality disorder	51	59.3	7	17.9[d]
History of psychiatric hospitalization	23	26.7	7	17.9
	Mean	*SD*	*Mean*	*SD*
Age (years)	31.1	9.7	29.9	7.7
Education (years)	13.3	2.6	14.2	2.2[e]
Socioeconomic status[f]	34.6	13.6	40.0	13.6[g]
Duration of index major depressive episode (weeks)	21.7	24.6	23.1	21.2
Age at onset of dysthymic disorder (years)	10.1	4.9		
Age at onset of major depressive disorder (years)	20.8	8.5	23.1	6.0

[a] For dysthymic patients, variable applies only to those who entered the study with a superimposed major depressive episode (N=50). Significant different between groups (p=0.04, Fisher's exact test).
[b] Nearly significant difference between groups (p=0.06, Fisher's exact test).
[c] Significant difference between groups (p=0.02, Fisher's exact test).
[d] Significant difference between groups (p<0.001, Fisher's exact test).
[e] Significant difference between groups (t=2.13, df=123, p<0.04).
[f] According to Hollingshead's Four Factor Index of Social Status (18).
[g] Nearly significant difference between groups (t=1.92, df=110, p<0.06).

Data Analysis

Group comparisons on baseline characteristics, onset of bipolar disorder, suicide attempts, and hospitalizations used chi-square and Fisher's exact tests for categorical variables and t tests for continuous variables. All tests were two-tailed. Recovery from and relapse into dysthymic disorder and major depressive episodes and risk of first lifetime major depressive episode were examined by using the life table method and the Kaplan-Meier estimator. Survival curves for the group with dysthymic disorder and the group with episodic major depressive disorder were compared by using the log-rank test. Data for patients who developed bipolar disorder were censored at the time of the first manic or hypomanic episode. Groups were compared on the proportions of the follow-up period at various levels of symptoms by using analysis of variance (ANOVA) and Tukey's honestly significant difference test. Scores on the modified Hamilton depression scale during follow-up were compared by using hierarchical linear models (27, 28). Group and time were treated as fixed effects, and the intercept was treated as a random effect. The best-fitting model incorporated autoregressive effects. Pairwise comparisons were conducted with Tukey-Kramer tests, which corrected for the number of comparisons. Finally, groups were compared on mean annual levels of treatment across the 5 years of follow-up by using repeated measures ANOVAs.

FIGURE 1. Survival Curve for Recovery Among 86 Patients With Dysthymic Disorder



We will provide data on the relationship between treatment and the course of dysthymic disorder in a future report. To briefly summarize, however, when we used Cox proportional hazards models treating levels of pharmacotherapy and psychotherapy as time-varying covariates, there were no significant associations between treatment and recovery from, or relapse into, dysthymic disorder. Ns varied slightly across analyses because of missing data.

Results

Patients' baseline characteristics appear in Table 1. Patients with episodic major depressive disorder had significantly more education than patients with dysthymic disorder. Significantly greater proportions of patients with dysthymic disorder than episodic major depressive disorder had a lifetime history of substance abuse or dependence and a comorbid personality disorder. Finally, patients with both dysthymic disorder and a lifetime history of major depressive disorder were significantly more likely to have recurrent major depressive episodes than were patients with episodic major depressive disorder.

Recovery From Dysthymic Disorder

Forty-three (50.0%) of the 86 patients with dysthymic disorder recovered during the course of the follow-up. After adjustment for censored observations, the estimated 5-year recovery rate was 52.9%, with a median time to recovery of 58 months (Figure 1). The rate of recovery was steepest in the first 7 months of follow-up, with an estimated 22.1% of the study group recovering during this period. Recoveries continued at a steady pace through month 34, with an estimated 46.5% of the study group recovering by this point. The recovery rate slowed substantially after month 35, with only an additional 7.0% of the study group recovering in the last 25 months of follow-up. The recovery rates of patients with dysthymic disorder

FIGURE 2. Survival Curve for Relapse Among 43 Patients Who Had Recovered From Dysthymic Disorder

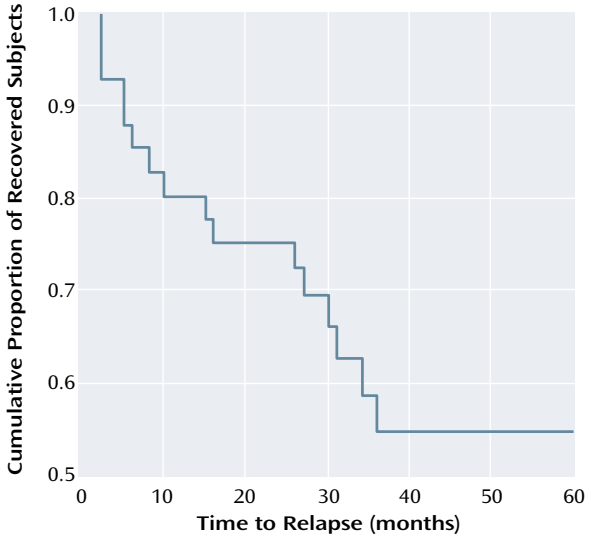
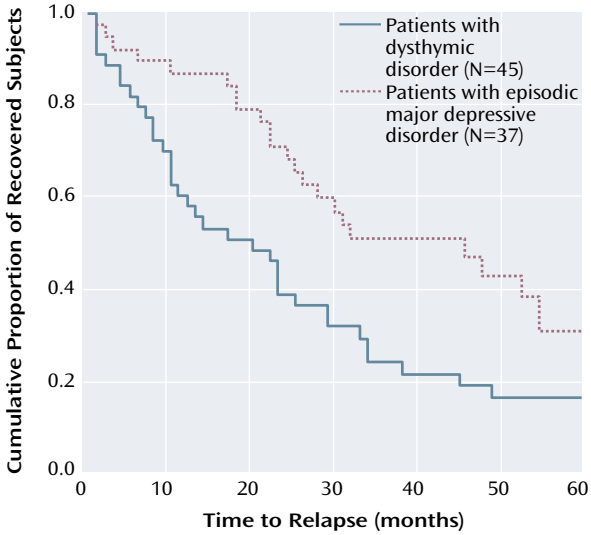


FIGURE 3. Survival Curves for Relapse Into a Major Depressive Episode Among Patients Who Had Recovered From an Index Episode[a]



[a]Groups differed significantly by log-rank test (p<0.01).

who entered the study with and without a superimposed major depressive episode did not differ. When we used more stringent criteria for recovery (26 weeks, rather than 8), 33 (38.4%) of the 86 patients with dysthymic disorder recovered, for an estimated 5-year recovery rate of 40.0%.

Relapse Into Dysthymic Disorder

Next, we examined relapse into dysthymic disorder for the 43 patients who had recovered. Relapse was defined as meeting the full DSM-III-R criteria for dysthymic disorder. The median interval between recovery from dysthymic disorder and the last follow-up was 47 months. By definition, the relapse had to begin at least 24 months before follow-up; hence, the median risk period for relapse was 23 months. Sixteen (37.2%) of the 43 patients relapsed during this period. After adjustment for censored observations, the estimated relapse rate was 45.2% (Figure 2). Relapse rates did not differ as a function of whether or not the patients entered the study with a superimposed major depressive episode. Finally, we examined relapse in the subset of 33 patients who met our more stringent (26-week) criteria for recovery. Requiring a longer period of recovery had little effect: 11 (33.3%) of these patients relapsed, yielding an estimated relapse rate of 39.1%.

Risk of Mania or Hypomania and First Major Depressive Episode

Five (5.8%) of the patients in the dysthymic disorder group but no patients in the episodic major depressive disorder group developed manic or hypomanic episodes during follow-up (p=0.32, Fisher's exact test). Two patients exhibited mood-congruent psychotic features during manic episodes and were hospitalized during the first year of follow-up. Three patients had hypomanic episodes, with the onsets of the first episodes distributed evenly across the follow-up period. The onset of manic or hypomanic episodes was not associated with the initiation of antidepressant medication in any case.

Nineteen of the 86 patients in the dysthymic disorder group reported never having had a major depressive episode in their lives at the initial evaluation. During the course of the 60-month follow-up, 14 (73.7%) of these patients experienced a first lifetime major depressive episode, yielding an estimated risk of 76.9% (median time to onset=33 months). The onsets of first lifetime major depressive episode were evenly distributed across the follow-up period.

Course of Superimposed Major Depressive Episodes

We previously reported that most patients who entered the study while in the midst of a major depressive episode had recovered by the 30-month follow-up (9). This pattern continued through the 60-month follow-up. Of the 50 patients with dysthymic disorder and a concurrent major depressive episode at entry into the study, 45 (90%) recovered from the major depressive episode, yielding an estimated recovery rate of 92.9% (median time to recovery=4 months). Two of the 39 patients with episodic major depression were partially recovered when they entered the study. All of the other 37 patients with episodic major depression recovered by 60 months (median time to recovery=3 months). Recovery rates did not differ significantly between groups.

The median period of risk for relapse into another major depressive episode (i.e., the interval between recovery from the index major depressive episode and the last follow-up) was 55 months for both the dysthymic disorder group and the episodic major depressive disorder group. Among the 45 patients with dysthymic disorder who re-

TABLE 2. Proportions of Follow-Up Period at Various Symptom Levels for Patients With Dysthymic Disorder and Patients With Episodic Major Depressive Disorder[a]

	Proportion of Time					
	Patients With Dysthymic Disorder				Patients With Episodic Major Depressive Disorder (N=39)	
	With Major Depressive Episode (N=50)		Without Major Depressive Episode (N=36)			
Symptom Level	Mean	SD	Mean	SD	Mean	SD
Mood disorder	0.72	0.33	0.63	0.36	0.23	0.28
Major depressive episode	0.40	0.36	0.21	0.26	0.11	0.12
Dysthymia (but not major depressive episode)	0.32	0.33	0.42	0.32	0.12	0.21
Well	0.18	0.28	0.27	0.30	0.65	0.30

[a] Proportions do not total 1 because many patients also experienced periods of subthreshold symptoms.

covered from their index major depressive episode, 35 (77.8%) relapsed by the 60-month follow-up, for an estimated relapse rate of 84.4% (median time to relapse=21 months) (Figure 3). Of the 37 patients with episodic major depressive disorder, 22 (59.5%) relapsed, for an estimated relapse rate of 70.2% (median time to relapse=47 months). The relapse rate was significantly higher among the patients with dysthymic disorder than among the patients with episodic major depressive disorder (log rank=6.72, df=1, p<0.01).

Although the numbers were small, we also examined the rates of a second prospectively observed recovery from, and relapse into, a major depressive episode. Among the 35 patients with dysthymic disorder and a superimposed major depressive episode at study entry who recovered and then relapsed into another major depressive episode, 27 (77.1%) recovered for a second time, for an estimated recovery rate of 88.6% (median time to recovery=5 months). Among the 22 patients with episodic major depressive disorder who recovered and then relapsed into another major depressive episode, 20 (90.9%) recovered for the second time, for an estimated recovery rate of 100% (median time to recovery=3 months). This difference was not quite significant (log rank=3.46, df=1, p=0.06).

Of the 27 patients with dysthymic disorder who recovered from a major depressive episode for the second time, 20 (74.1%) experienced another relapse, for an estimated relapse rate of 93.2% (median time to relapse=9 months). Of the 20 patients with episodic major depressive disorder who recovered from a major depressive episode for the second time, nine (45.0%) experienced another relapse, for an estimated relapse rate of 67.1% (median time to relapse=30 months) (log rank=8.52, df=1, p<0.004).

Proportion of Follow-Up Period at Various Symptom Levels

To summarize the patients' course across the entire follow-up period, we computed the proportion of time that they met the full symptom criteria for a mood disorder, major depressive disorder, or dysthymic disorder (but no superimposed major depressive episode) and were completely recovered from all mood disorders (Table 2). Patients with dysthymic disorder who entered the study with a superimposed major depressive episode, patients with dysthymic disorder who did not have a superimposed major depressive episode at study entry, and patients with episodic major depressive disorder differed significantly on the proportions of the follow-up period they spent meeting the symptom criteria for a mood disorder (F=27.14, df=2, 122, p<0.001), major depressive disorder (F=12.69, df=2, 122, p<0.001), dysthymic disorder (F=10.04, df=2, 122, p<0.001), and on the time spent recovering from all mood disorders (F=29.58, df=2, 122, p<0.001). Pairwise comparisons indicated that both subgroups of patients with dysthymic disorder spent a significantly greater proportion of the follow-up period with a mood disorder or meeting the symptom criteria for dysthymic disorder and significantly less of the follow-up period recovered from all mood disorders than did patients with episodic major depressive disorder. Patients with dysthymic disorder who entered the study in a superimposed major depressive episode also spent a significantly greater proportion of the follow-up period in a major depressive episode than did patients with dysthymic disorder without superimposed major depressive episodes at entry into the study and patients with episodic major depressive disorder.

TABLE 3. Scores on 24-Item Modified Hamilton Depression Scale for Patients With Dysthymic Disorder and Patients With Episodic Major Depressive Disorder

	Score on Hamilton Depression Scale					
	Patients With Dysthymic Disorder				Patients With Episodic Major Depressive Disorder (N=39)	
	With Major Depressive Episode (N=50)		Without Major Depressive Episode (N=36)			
Time	Mean	SD	Mean	SD	Mean	SD
Baseline	32.2	8.2	16.9	6.2	30.5	7.7
30 months	21.2	11.0	15.2	8.7	6.8	6.0
60 months	21.3	12.8	16.6	10.7	9.0	7.6

Modified Hamilton Depression Scale

The three groups' scores on the modified Hamilton depression scale at baseline and at the 30- and 60-month assessments appear in Table 3. There were significant effects for group (F=28.64, df=2, 139, p<0.001), time (F=94.66, df=2, 218, p<0.001), and interaction of group and time (F=25.24, df=4, 218, p<0.001). Pairwise comparisons indicated that patients with dysthymic disorder with a superimposed major depressive episode and patients with epi-

sodic major depressive disorder both entered the study with significantly higher scores on the modified Hamilton depression scale than did patients with dysthymic disorder without a superimposed major depressive episode. At 30 months, scores on the modified Hamilton depression scale for patients with dysthymic disorder with a superimposed major depressive episode at baseline and patients with episodic major depressive disorder had decreased significantly, whereas scores on the modified Hamilton depression scale for patients with dysthymic disorder without a superimposed major depressive episode at baseline were unchanged. Although the difference between the two dysthymic disorder groups was no longer significant at 30 months, both dysthymic disorder groups were significantly more depressed than the patients with episodic major depressive disorder. Finally, none of the groups exhibited significant changes in scores on the modified Hamilton depression scale between the 30- and 60-month follow-ups. At 60 months, the two dysthymic disorder groups did not differ on scores on the modified Hamilton depression scale, but both continued to experience significantly higher levels of depression than did patients with episodic major depressive disorder.

Mortality and Suicide Attempts

Three patients died during the 60-month follow-up period. Two patients with episodic major depressive disorder died of natural causes, and one patient with dysthymic disorder committed suicide. During the follow-up, suicide attempts were made by 19.0% (16 of 84—data were missing for two subjects) of the patients with dysthymic disorder but none of the 37 patients with episodic major depressive disorder (p=0.003, Fisher's exact test). The patients with dysthymic disorder with and without superimposed major depressive episodes at entry into the study did not differ on numbers of suicide attempts.

Hospitalization

During the follow-up, 22.4% (19 of 85) of the patients with dysthymic disorder had one or more psychiatric hospitalizations compared to 2.7% (one of 37) of the patients with episodic major depressive disorder (p=0.007, Fisher's exact test). Patients with dysthymic disorder with and without superimposed major depressive episodes at entry into the study did not differ on the number of hospitalizations.

Outpatient Treatment

At the end of the first year of follow-up, 50.0% (43 of 86) of the patients with dysthymic disorder were receiving outpatient mental health treatment. This proportion declined slightly over the follow-up period, with 45.3% (N=39) receiving outpatient treatment at the end of the third year and 40.7% (N=35) receiving treatment at the end of the fifth year of follow-up. Only a minority of the patients received a definitely or probably adequate level of antidepressant medication: 25.6% (N=22), 24.4% (N=21), and 30.2% (N=26) at the end of years 1, 3, and 5, respectively. The number of patients receiving psychotherapy on a weekly or biweekly basis declined gradually over the course of the follow-up, from 38.4% (N=33) at the end of the first year to 27.9% (N=24) at the end of the third year to 23.3% (N=20) at the end of the fifth year.

To analyze these data more formally, we compared the groups' mean treatment scores for antidepressant medication and psychotherapy for each 12-month interval throughout the follow-up. For medication, there was a significant effect for group, with the patients with dysthymic disorder (mean=0.72, SD=0.85) receiving significantly higher levels of medication than the patients with episodic major depressive disorder (mean=0.27, SD=0.57) ($F=8.63$, $df=1, 109$, $p=0.004$). Neither the main effect for time nor the interaction of group and time was significant. For psychotherapy, the main effect for group was marginally significant, with the patients with dysthymic disorder (mean=1.06, SD=0.93) receiving more psychotherapy than the patients with episodic major depressive disorder (mean=0.72, SD=0.76) ($F=3.90$, $df=1, 109$, $p=0.05$). In addition, there was a significant main effect for time ($F=9.73$, $df=4, 436$, $p<0.001$), reflecting a linear decrease in the mean level of psychotherapy in both groups over the course of the follow-up. The interaction of group and time was not significant. The subgroups of patients with dysthymic disorder with and without superimposed major depressive episodes at entry into the study did not differ on levels of pharmacotherapy and psychotherapy during the follow-up period.

Discussion

This article describes the 5-year course and outcome of early-onset dysthymic disorder. To our knowledge, this is the longest prospective, naturalistic follow-up study of adults with dysthymic disorder in the literature. It extends our previous 30-month follow-up (9) by providing the first published data on the risk of relapse in dysthymic disorder and provides an additional 30 months of data on recovery, outcome, the risk of bipolar disorder and first major depressive episode, the course of superimposed major depressive episodes, suicidality, and treatment.

The probability of recovery from dysthymic disorder increased slowly throughout the first 35 months of follow-up and then leveled off. Even after 5 years, only about half of the patients had recovered, according to the liberal criteria of the Longitudinal Interval Follow-Up Evaluation of at least 8 consecutive weeks with minimal or no symptoms. When we used more stringent criteria for recovery (26 weeks), the estimated recovery rate was 40.0% after 5 years.

Although we had only a median of 23 months to observe relapse, an estimated 45.2% of the study group relapsed, meeting the full criteria for dysthymic disorder. This is probably an underestimate, because several additional

patients experienced a recurrence of symptoms that appeared to be persistent but had not lasted the required 24 months at the time of follow-up. The high relapse rate is not attributable to brief remissions, because requiring a recovery of 6 (rather than 2) months did not produce a substantially lower relapse rate. These data indicate that patients who recover from dysthymic disorder are at high risk for relapse and highlight the importance of developing effective strategies for long-term treatment (29, 30).

We contrasted the group with dysthymic disorder with a "near-neighbor" comparison group of patients with episodic major depressive disorder. The data indicated that although dysthymic disorder often presents with only mild to moderate symptoms, from a longitudinal perspective, it is more severe than episodic major depressive disorder, at least in outpatient settings, and constitutes a significant public health problem. Over the course of the 5-year follow-up, the patients with dysthymic disorder spent approximately 70% of the time meeting the criteria for a mood disorder compared to less than 25% of the time for the patients with episodic major depressive disorder. Consistent with these findings, the patients with dysthymic disorder exhibited clinically significant levels of depression on the modified Hamilton depression scale at both the 30- and 60-month follow-ups—differing significantly from the patients with episodic major depressive disorder. In addition, a significantly greater proportion of the patients with dysthymic disorder than the patients with episodic major depressive disorder attempted suicide and had psychiatric hospitalizations during the follow-up period. By the same token, these data indicate that purely episodic forms of major depressive disorder also exhibit a consistent, albeit more benign, course.

Another important finding was that an estimated 73.7% of the patients with dysthymic disorder who reported never experiencing a major depressive episode in the initial evaluation developed a first lifetime major depressive episode within 5 years of follow-up. Because 77.9% (67 of 86) of the dysthymic disorder group had already experienced a superimposed major depressive episode by the beginning of the study, 94.2% (81 of 86) of the group had at least one lifetime major depressive episode by the end of the 5-year follow-up. These data extend our previous finding that 42% of the patients with "pure" dysthymic disorder developed a first lifetime major depressive episode within 30 months of follow-up (9) and suggest that almost all individuals with dysthymic disorder will eventually experience a major depressive episode at some point in their lives. At the same time, we found few differences in course and outcome between patients with dysthymic disorder with and without superimposed major depressive episodes at entry into the study. Taken together, these data indicate that dysthymic disorder and "double depression" (8) should probably be conceptualized as the same condition viewed at different points in their course. Because double depression and chronic major depressive disorder are also similar with regard to most clinical characteristics, family history, and pharmacological response (31), dysthymic disorder may be part of an even larger group of chronic depressive conditions with similar features and correlates.

A small number of patients with dysthymic disorder developed bipolar disorder during follow-up. Manias tended to develop early, whereas hypomanias were evenly distributed across the follow-up period. Although the proportion of patients developing bipolar disorder was higher in the dysthymic disorder group than in the episodic major depressive disorder group, the difference was not statistically significant.

Given the high comorbidity between dysthymic disorder and major depressive disorder, knowledge of the course of major depressive episodes in dysthymic disorder is important. We found that almost all patients with dysthymic disorder recovered from superimposed major depressive episodes, but most relapsed quickly. We extended the findings from our previous report (9) to include second prospectively observed recoveries from, and relapses into, major depressive episodes. Rates of recovery from the first and second major depressive episodes were similar; however, second relapses tended to be faster than first relapses. This may be because of a progressive shortening of interepisode intervals over time, or it may reflect a differential sieve process, with the patients who had already relapsed once during follow-up comprising a subgroup with a particularly high propensity for relapse. Compared to the patients with episodic major depressive disorder, the patients with dysthymic disorder recovered nonsignificantly more slowly from major depressive episodes but relapsed significantly more quickly. It is notable that these findings were evident for both the first and second prospectively observed major depressive episodes.

Only a minority of the patients with dysthymic disorder were in treatment at any given time during the follow-up. Approximately 25%–30% of the dysthymic disorder group received adequate or probably adequate pharmacotherapy. This proportion was stable across the follow-up, although without further analyses, it is unclear whether this is because the same patients were taking medication for extended periods or because the number of patients dropping out of treatment was similar to the number reentering treatment in any given period. The number of patients with dysthymic disorder receiving weekly or biweekly psychotherapy declined over time. Further analyses are necessary to determine whether the patients terminated psychotherapy because they had remitted, were discouraged by a lack of improvement, or for other reasons (e.g., financial or insurance constraints). It is interesting that the patients with dysthymic disorder received significantly more treatment than did the patients with episodic major depressive disorder across the follow-up period. Thus, treatment probably cannot account for the poorer course and outcome of the dysthymic disorder group. Rather, it is

likely that the patients with dysthymic disorder received higher levels of treatment because of their continuing symptoms.

This study has a number of strengths, including a larger study group and a longer follow-up period than those that have been previously reported, repeated follow-up evaluations using semistructured clinical interviews, comparisons of patients with dysthymic disorder with and without a superimposed major depressive episode, and the use of a near-neighbor comparison group of patients with episodic major depressive disorder. However, the study also has several limitations. First, we asked patients to report after relatively lengthy follow-up intervals. Although long follow-up intervals are appropriate for chronic conditions, it would be prudent to regard the data on patient recovery and relapse as approximations. Second, the study group was limited to patients with early-onset dysthymic disorder; hence, the results may not apply to late-onset cases. Finally, our treatment data were limited in that we could not assess the quality of psychotherapy and patients' compliance with treatment. We are continuing to follow up this study group at 7.5 and 10 years after entry into the study to provide data on the long-term course and outcome of dysthymic disorder.

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