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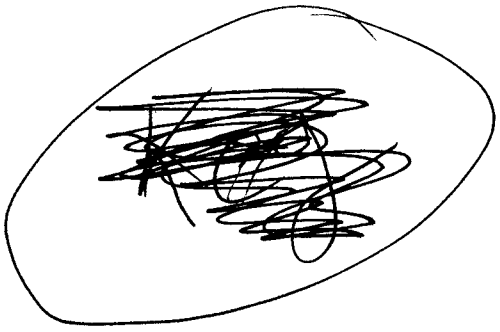

American Psychiatric Foundation
AJP: THE AMERICAN JOURNAL OF PSYCHIATRY
Official Journal of the American Psychiatric Association

Characteristics and Significance of Untreated Major Depressive Disorder

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Volume 152(8), August 1995, pp 1124-1129
[Regular Articles]

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Abstract

Objective: This study sought to describe the characteristics and consequences of untreated major depressive disorder. Method: As part of a family study of probands with major affective disorders, raters assessed 3,119 first-degree relatives, spouses, and comparison subjects. When 2,237 (71.7%)

Outline

Graphics

of these individuals were reassessed 6 years later, 547 had experienced episodes of major depressive disorder in the interval. Those who had sought any form of treatment for any episode of major depressive disorder in the interval were compared, by baseline demographic characteristics and clinical features of their worst episodes of major depressive disorder, to those who had not. Individuals who had had untreated major depressive disorder were then compared, by changes in socioeconomic status and by levels of psychosocial impairment at follow-up, to a matched group with no major depressive disorder in the interval. Results: The worst episodes of 313 treated individuals, compared to those of 234 untreated individuals, were characterized by older age, symptoms of the endogenous subtype, longer durations, and the presence of disruption in role function. Each of these factors contributed independently to the distinction between treated and untreated episodes. Untreated individuals experienced significant psychosocial impairment on follow-up but did not show the economic disadvantages shown elsewhere for probands who began follow-up as they sought treatment at tertiary medical centers. Conclusions: These data suggest that illness characteristics and age determine the decision to seek treatment for major depressive disorder. Untreated depression is apparently associated with long-standing psychosocial difficulties but not with serious economic consequences. (Am J Psychiatry 1995; 152:1124-1129)

American surveys over the past 15 years have shown that fewer than one-half of those who develop depressive episodes seek treatment for them [1-5]. Because nearly all the literature describing affective disorder is based on treated samples, we know very little about the larger group with depression but without treatment. The few studies attempting to characterize this group have reached little consensus. Two of these associated treatment seeking with female sex [1,2], and two found that married individuals were less likely to obtain treatment [2,4]. Two studies have also agreed that sleep difficulties, feelings of guilt, and suicidal ideation are more frequent in treated groups [4,5].

The only nationwide survey available estimated the lifetime prevalence of major depressive disorder in the United States to be 17.1% [6]. Questions concerning those who are untreated therefore have great public health significance. The following analyses considered, first, the demographic and clinical differences between those who did, and those who did not, seek treatment for major depressive disorder that was present during the 6-year follow-up of a large, nonclinical cohort.

It is intuitively likely that severity or duration of illness and the resulting disability will be among the more important factors separating treated from untreated individuals. This leaves the important second question of how much impairment those with untreated depression have. The Research Diagnostic Criteria (RDC) [7], DSM-III, and DSM-III-R all require some level of illness-associated impairment for the diagnosis of major depressive disorder, but this impairment need not be severe. If untreated episodes are generally so brief or mild that the associated impairment does not result in measurable changes in psychosocial functioning, then the fact that so many depressed individuals do not get treatment would be less troublesome. If, on the other hand, untreated depression can be shown to result in substantial and lasting dysfunction, access to treatment would become an important focus for remediation.

METHOD

Earlier reports have described this cohort and study design [8,9]. As part of the National Institute of Mental Health Program on the Psychobiology of Depression--Clinical Studies, 616 probands who were seeking treatment for major depressive disorder, mania, or schizoaffective disorder, according to Research Diagnostic Criteria [7], entered a family study. Of those first-degree relatives and current spouses who were alive and over 17 years of age, 76% (N=2,306) and 77% (N=344),

respectively, were interviewed by raters blind to proband diagnosis. In addition, 469 individuals were recruited from the community through an acquaintanceship method as age- and sex-matched comparison subjects for a randomly selected subset of relatives [10]. All subjects provided informed consent.

Raters used informants, medical records, and the Schedule for Affective Disorders and Schizophrenia (SADS-L) [11] to assess current and lifetime psychopathology for all relatives, comparison subjects, and spouses. They used the Personal History of Depressive Disorders (available on request from Dr. Coryell) to obtain detailed demographic data. This instrument included Hollingshead and Redlich ratings of occupational and educational status [12].

Of 3,119 relatives, comparison subjects, and spouses initially interviewed, 2,237 (71.7%) were reinterviewed 6 years later. Assessments at that time included the SADS-L-Interval form (SADS-LI), an instrument modified from the SADS-L to describe in greater detail any psychopathology that had occurred in the preceding interval. Raters also used the Longitudinal Interval Follow-Up Evaluation--Base Psychosocial Schedule, a modification of the Longitudinal Interval Follow-Up Evaluation [13], to quantify the impact of psychopathology on specific areas of psychosocial functioning. This instrument includes the Global Assessment Scale (GAS), a rating that assigns a single score to reflect both level of functioning and symptom intensity [14].

Impairment due to psychopathology was noted for performance at work, in household duties, and in student activities. The remaining areas--recreational activities, sexual activity, overall satisfaction, overall social adjustment, and interpersonal relationships with spouses, other family members, and friends--were rated according to level of functioning regardless of whether or not impairment had resulted from psychopathology. Interpersonal functioning and sexual activity were rated for the month preceding the follow-up interviews. Otherwise, ratings applied to the preceding week.

To contrast individuals with depression who did not seek treatment with depressed individuals who did, we identified all those relatives, comparison subjects, and spouses who reported an episode of major depressive disorder beginning after the initial interview but before the follow-up interview 6 years later. Individuals who received psychotherapy, ECT, or medication as treatment for an episode of major depressive disorder in the follow-up interval, or who were hospitalized for any problems thought to result from major depressive disorder, were included in the "treated" group. Thus, individuals in this group were not necessarily treated for all episodes, and the treatments received were not necessarily adequate or appropriate. Moreover, before intake, some untreated individuals may have had episodes for which they had been treated. Treatment received for problems other than major depressive disorder did not qualify the individual for inclusion in the treated group.

Using the demographic measures assessed at the first interview, we compared those who had and those who had not obtained treatment for any episode. We next compared groups by the duration, symptoms, and impairment characterizing the most severe episode in the interval. Finally, we compared groups by lifetime diagnoses, as apparent at the follow-up interview.

Our second question concerned the degree of impairment experienced by those with untreated major depressive disorder. To address this, we identified all those who reported any major depressive disorder during the follow-up interval, regardless of onset date, and who obtained no treatment for any episode. In order to quantify impairment in a manner directly analogous to that used in an earlier study of probands [14], each individual was matched by sex and age to an individual who reported no major depressive disorder in the follow-up interval. Groups were then compared by baseline demographic characteristics and by changes over that interval in marital status, occupational status, educational level, and household income. Finally, groups were compared by ratings on the Longitudinal Interval Follow-Up Evaluation--Base Psychosocial Schedule obtained at the follow-up interview.

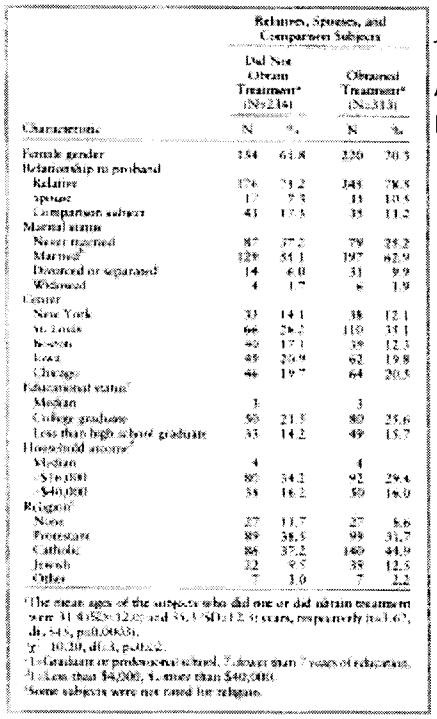
Group comparisons used t tests for dimensional variables and chi-square tests for categorical variables. Hierarchical regression analyses tested the relative importance of differences that emerged as significant in the univariant analyses. In all

tests, statistical significance was defined as alpha <=0.05.

RESULTS

Of 547 individuals who described an episode of major depressive disorder beginning in the 6-year interval between the first and second interviews, 313 (57.2%) were included in the treated group. Of those, 106 (33.9%) had received psychotherapy alone.

Treated individuals were significantly older and were more likely to be married than were untreated individuals (Table 1). The groups did not differ by sex, center, educational level, household income, or religious preference.



Characteristic	Relatives, Spouses, and Comparison Subjects			
	Did Not Obtain Treatment* (N=234)		Obtained Treatment* (N=313)	
	N	%	N	%
Female gender	154	65.8	220	70.3
Relationship to proband				
Relative	176	75.2	245	78.3
Spouse	17	7.3	33	10.5
Comparison subject	41	17.5	35	11.2
Marital status				
Never married	87	37.2	79	25.2
Married[a]	129	55.1	197	62.9
Divorced or separated	14	6.0	31	9.9
Widowed	4	1.7	6	1.9
Center				
New York	33	14.1	38	12.1
St. Louis	66	28.2	110	35.1
Boston	40	17.1	39	12.5
Edmonton	49	20.9	62	19.8
Chicago	46	19.7	64	20.5
Educational status[b]				
Median	3		3	
College graduate	50	21.5	80	25.6
Less than high school graduate	33	14.2	49	15.7
Household income[c]				
Median	4		4	
<$16,000	80	34.2	92	29.4
>$40,000	38	16.2	50	16.0
Religion[d]				
None	27	11.7	27	8.6
Protestant	89	38.5	99	31.7
Catholic	86	37.2	140	44.9
Jewish	22	9.5	39	12.5
Other	7	3.0	7	2.2

[a] The mean ages of the subjects who did not obtain treatment were 31.9 (SD=12.2) and 35.3 (SD=12.9) years, respectively (t=3.62, df=545, p=0.0003).
[b] χ^2=10.29, df=3, p=0.02.
[c] 1=Graduate or professional school, 2=some college, 3=high school graduate, 4=some high school, 5=8 years of education or less.
[d] 1=Less than $8,000, 4=more than $40,000.
[e] Some subjects were not rated for religion.

Table 1. Demographic Characteristics of Relatives and Spouses of Subjects With Major Affective Disorders and Comparison Subjects With Onset of Untreated or Treated Major Depressive Disorder During 6-Year Follow-Up

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Treated and untreated individuals did not differ significantly by their relationship to probands when relatives, spouses, and comparison subjects were grouped separately. However, spouses and relatives had in common a familiarity with the proband, and, consequently, there was a higher likelihood that that exposure might have influenced treatment-seeking behavior. The combined group of spouses and relatives, in fact, was significantly more likely to seek treatment than were comparison subjects; 278 (59.0%) of the relatives and spouses with major depressive disorder and 35 (46.0%) of the comparison subjects with major depressive disorder sought treatment (chi squared=4.50, df=1, p=0.03).

Treated and untreated individuals experienced nearly identical mean numbers of episodes of major depressive disorder during the follow-up interval (mean=2.2, SD= 3.4, and mean=2.2, SD=4.3, respectively). However, untreated individuals had had fewer episodes before intake than had treated individuals (mean=2.1, SD=7.7, and mean=3.6, SD=9.8, respectively) (t=-2.1, df=543.6, p=0.04). The two groups were not significantly dissimilar in the number of subjects with alcoholism, drug abuse, phobic disorder (excluding agoraphobia), intermittent depressive disorder, or chronic minor depressive disorder in the interval. The treated group was significantly more likely to have manifested panic disorder or agoraphobia; 17 (5.4%) of the

subjects in the treated group and four (1.7%) in the untreated group manifested either or both syndromes during the follow-up interval (chi squared=5.0, df=1, p=0.03).

Treated individuals reported having had significantly more criteria depressive symptoms during their worst episode (Table 2). While approximately half of each group experienced at least some role-function impairment noticeable to others, a "disruption" (cessation) of the individual's principal social role functioning was three times more likely among the treated individuals. Treated individuals were nearly seven times more likely to have been completely incapacitated by their worst episode. Moreover, the median duration of the longest episode among the treated individuals was more than three times that of the untreated individuals.

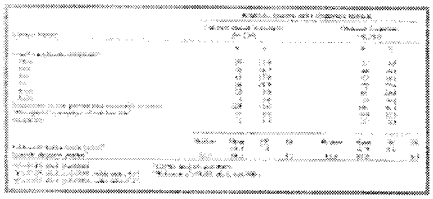

Table 2. Clinical Features of the Most Severe Episode of Major Depressive Disorder of Relatives and Spouses of Subjects With Major Affective Disorders and Comparison Subjects With Onset of Untreated or Treated Major Depressive Disorder During 6-Year Follow-Up

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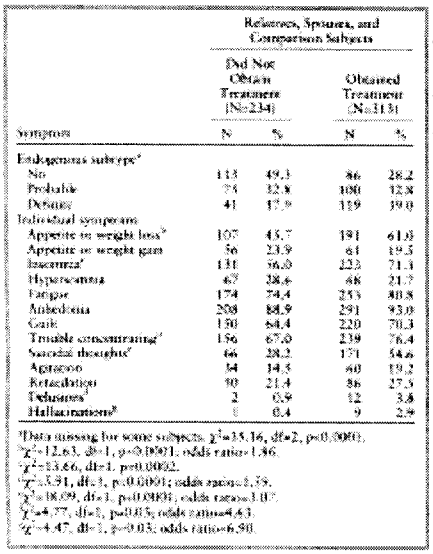
Symptoms associated with the RDC endogenous subtype were significantly more common during the most severe episodes of those individuals who sought treatment (Table 3). They were twice as likely as untreated individuals to have met definite RDC for the endogenous subtype.



	Relatives, Spouses, and Comparison Subjects			
	Did Not Obtain Treatment (N=234)		Obtained Treatment (N=313)	
Symptom	N	%	N	%
Endogenous subtype[a]				
No	113	49.3	86	28.2
Probable	74	32.8	100	32.8
Definite	41	17.9	119	39.0
Individual symptoms				
Appetite or weight loss[b]	107	45.7	191	61.0
Appetite or weight gain	56	23.9	61	19.5
Insomnia[c]	131	56.0	223	71.3
Hypersomnia	67	28.6	68	21.7
Fatigue	174	74.4	253	80.8
Anhedonia	208	88.9	291	93.0
Guilt	150	64.4	220	70.3
Trouble concentrating[d]	156	67.0	239	76.4
Suicidal thoughts[e]	66	28.2	171	54.6
Agitation	34	14.5	60	19.2
Retardation	50	21.4	86	27.5
Delusions[f]	2	0.9	12	3.8
Hallucinations[g]	1	0.4	9	2.9

[a] Data missing for some subjects. $\chi^2=35.16$, df=2, p<0.0001.
[b] $\chi^2=12.63$, df=1, p=0.0021; odds ratio=1.86.
[c] $\chi^2=13.66$, df=1, p=0.0002.
[d] $\chi^2=5.91$, df=1, p=0.0001; odds ratio=2.59.
[e] $\chi^2=16.09$, df=1, p=0.0001; odds ratio=3.07.
[f] $\chi^2=4.77$, df=1, p=0.05; odds ratio=4.43.
[g] $\chi^2=4.47$, df=1, p=0.03; odds ratio=6.90.

Table 3. Quality of Depressive Symptoms of Relatives and Spouses of Subjects With Major Affective Disorders and Comparison Subjects With Onset of Untreated or Treated Major Depressive Disorder During 6-Year Follow-Up

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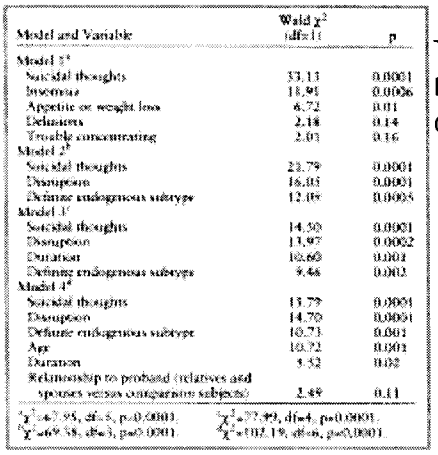
The first logistic regression model tested those depressive symptoms which, in the univariant analysis, discriminated the two groups at at least the 0.05 level (Table 4). Appetite or weight loss, insomnia, and suicidal thoughts remained significant,

while "trouble concentrating" and the presence or absence of delusions did not. Because the endogenous subtype seemed to capture most phenomenological differences between the groups, we entered this subtype, suicidal thoughts, and role disruption in the second model. All three variables were highly significant predictors of treatment-seeking behavior after control for the others. Duration, and then age and relationship to proband (relatives and spouses versus comparison subjects), were added in successive models. Duration and age, but not relationship to proband, were significantly and independently related to treatment-seeking behavior. Disruption and the endogenous subtype remained significant, but the presence of suicidal thoughts was the most robust predictor in all models.



Model and Variable	Wald χ^2 (df=1)	p
Model 1[a]		
Suicidal thoughts	33.13	0.0001
Insomnia	18.95	0.0026
Appetite or weight loss	6.72	0.01
Delusions	2.18	0.14
Trouble concentrating	2.01	0.16
Model 2[b]		
Suicidal thoughts	23.79	0.0001
Disruption	16.05	0.0001
Defines endogenous subtype	12.09	0.0005
Model 3[c]		
Suicidal thoughts	14.50	0.0001
Disruption	13.97	0.0002
Duration	10.69	0.001
Defines endogenous subtype	9.46	0.002
Model 4[d]		
Suicidal thoughts	13.79	0.0001
Disruption	14.70	0.0001
Defines endogenous subtype	10.73	0.001
Age	10.72	0.001
Duration	5.52	0.02
Relationship to proband (relatives and spouses versus comparison subjects)	2.49	0.11

[a] χ^2=2.95, df=5, p=0.0800. [b] χ^2=77.99, df=4, p=0.0001. [c] χ^2=69.58, df=3, p=0.0001. [d] χ^2=102.19, df=6, p=0.0001.

Table 4. Logistic Regression Analyses of Depressive Episodes and Treatment-Seeking Behavior of Relatives and Spouses of Subjects With Major Affective Disorders and Comparison Subjects With Onset of Major Depressive Disorder During 6-Year Follow-Up

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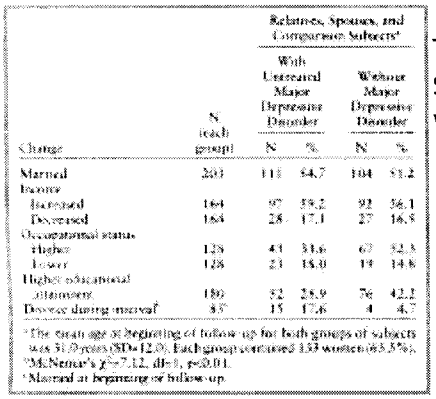
Matching procedures yielded 203 individuals with untreated major depressive disorder, and a corresponding 203 with no major depressive disorder, in the follow-up interval (Table 5). In 31 instances, one or the other member of a matched pair lacked ratings on one of the relevant instruments--the Longitudinal Interval Follow-Up Evaluation-II, the SADS-LI, or the Personal History of Depressive Disorders. Changes in occupational and educational status over the 6-year follow-up favored subjects who had experienced no major depressive disorder, but differences were not statistically significant. However, those with untreated depression were more than three times more likely to have obtained a divorce during the interval.



		Relatives, Spouses, and Comparison Subjects[a]			
		With Untreated Major Depressive Disorder		Without Major Depressive Disorder	
Change	N (each group)	N	%	N	%
Married	203	113	54.7	104	51.2
Income					
Increased	164	97	59.2	92	56.1
Decreased	164	28	17.1	27	16.5
Occupational status					
Higher	128	41	31.6	67	52.3
Lower	128	23	18.0	19	14.8
Higher educational attainment	180	52	28.9	76	42.2
Divorce during interval[b]	85	15	17.6	4	4.7

[a] The mean age at beginning of follow-up for both groups of subjects was 31.0 years (SD=12.0). Each group contained 133 women (65.5%). [b] McNemar's χ^2=7.12, df=1, p=0.01. [c] Married at beginning of follow-up.

Table 5. Changes in Socioeconomic Status at Follow-Up for Relatives and Spouses of Subjects With Major Affective Disorders and Comparison Subjects With Untreated and Without Major Depressive Disorder During 6-Year Follow-Up

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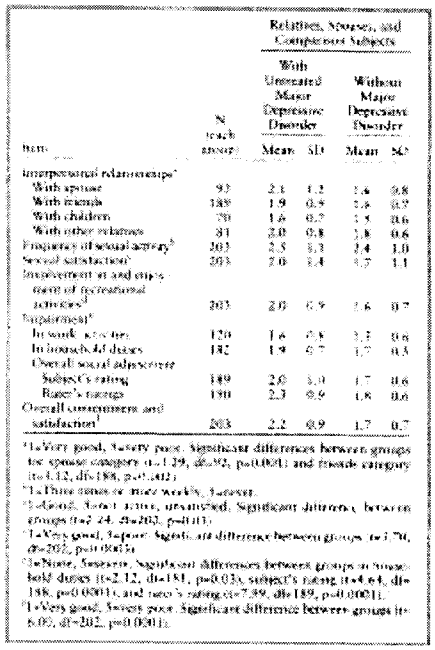
Those who had had an untreated depression described significantly more impairment during the final 6 months of the 6-year follow-up (Table 6). This was true of relationships with spouses and friends, the enjoyment of recreational activities, sexual satisfaction, and performance of household duties. Global ratings of social adjustment and overall contentment showed a particularly marked difference between those with untreated depression and those without depression. Notably, though, those with untreated depression did not describe greater impairment at work or less frequency of sexual activity at the time of follow-up, and impairment in household duties was only weakly significant.



		Relatives, Spouses, and Comparison Subjects			
		With Untreated Major Depressive Disorder		Without Major Depressive Disorder	
Item	N (each group)	Mean	SD	Mean	SD
Interpersonal relationships[a]					
With spouse	92	2.1	1.2	1.6	0.8
With friends	185	1.9	0.9	1.6	0.7
With children	70	1.6	0.7	1.5	0.6
With other relatives	81	2.0	0.8	1.8	0.6
Frequency of sexual activity[b]	203	2.5	1.3	2.4	1.0
Sexual satisfaction[c]	203	2.0	1.4	1.7	1.1
Involvement in and enjoyment of recreational activities[d]	203	2.0	0.9	1.6	0.7
Impairment[e]					
In work activities	120	1.6	0.8	1.3	0.6
In household duties	182	1.9	0.7	1.7	0.5
Overall social adjustment					
Subject's rating	189	2.6	1.0	1.7	0.6
Rater's ratings	190	2.3	0.9	1.6	0.6
Overall contentment and satisfaction[f]	203	2.2	0.9	1.7	0.7

[a] 1=Very good, 5=very poor. Significant differences between groups for spouse category ($t=4.39$, $df=92$, $p<0.0001$) and friends category ($t=4.12$, $df=188$, $p<0.0001$).
[b] 1=Three times or more weekly, 5=never.
[c] 1=Good, 5=not at all, unsatisfied. Significant difference between groups ($t=2.24$, $df=203$, $p<0.03$).
[d] 1=Very good, 5=poor. Significant difference between groups ($t=3.70$, $df=202$, $p<0.0003$).
[e] 1=None, 5=severe. Significant differences between groups in household duties ($t=2.12$, $df=181$, $p<0.03$), subject's rating ($t=6.64$, $df=188$, $p<0.0001$), and rater's rating ($t=7.89$, $df=189$, $p<0.0001$).
[f] 1=Very good, 5=very poor. Significant difference between groups ($t=6.05$, $df=202$, $p<0.0001$).

Table 6. Psychosocial Impairment During Final 6-Months of Follow-Up for Relatives and Spouses of Subjects With Major Affective Disorders and Comparison Subjects With Untreated and Without Major Depressive Disorder During 6-Year Follow-Up

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To test whether the more severely affected among the untreated individuals had experienced substantial impairment, we identified those whose episodes had persisted beyond the group median duration of 8 weeks and who had had, in addition, five or more criteria depressive symptoms. This more severely affected subgroup was significantly more likely to have experienced a decrease in occupational status during follow-up than were the matched comparison subjects (N=12 (30.0%) of 67 versus 3 (7.5%) of 67; McNamara's chi squared=4.92, df= 1, $p<0.05$). Otherwise, differences between these individuals and the matched comparison subjects were not greater than the differences between individuals in the overall group and their comparison subjects. In fact, in no comparison of the variables listed in (Table 6) was the disparity between the depressed and nondepressed individuals greater for the "severe" subgroup than it was for the group with untreated depression as a whole.

DISCUSSION

Among demographic measures, only age and marital status significantly distinguished those who sought treatment for major depressive disorder from those who did not. That older individuals were more likely to seek treatment accords with the findings of Bucholz and Robins [2] and Bucholz and Dinwiddie [3] but contradicts Weissman et al [1]. Moreover, those who were not married at baseline were more likely to seek treatment, rather than less likely to seek treatment, as they were in the studies of Bucholz and Robins [2], Bucholz and Dinwiddie [3], and Dew et al [4]. Thus, the present study does not add to

the limited consistency with which demographic factors predict treatment-seeking behavior in major depressive disorder.

Those whose depression resulted in impairment in major life-role performance were not more likely to seek treatment than were other depressed subjects. Not surprisingly, a cessation of role functioning was powerfully associated with treatment-seeking behavior. Longer durations were also characteristic of the treated group, independent of life-role disruption. This may seem counterintuitive because many treated individuals received medications or psychotherapies designed to shorten episodes. The findings highlight the fact that major depressive disorder is, in the large majority of cases, a self-limiting condition. Individuals who experience episodes that are both persistent and disabling are likely to be grossly overrepresented in treatment-seeking samples, and this may foster the impression among clinicians that the resolution of depressive symptoms is primarily treatment dependent. This finding also suggests that many individuals who appear to be placebo responsive are not, in fact, responding but are manifesting the natural course of their illness.

Symptoms traditionally associated with the endogenous subtype of depression were also much more common among those who sought treatment. Because this effect remained robust after control for both duration and role disruption, it indicates that individuals view some symptoms, more than other symptoms, as indicative of a need for treatment. It is probably no coincidence that these are the same symptoms long considered by clinicians as indications of a nonsituational disorder in need of somatic therapy.

Many of these individuals had, at the beginning of the follow-up interval, exposure to a family member who was seeking treatment for an affective disorder. This exposure undoubtedly increased the likelihood that they would seek treatment when they themselves developed affective symptoms. However, among the significant correlates of treatment seeking described here, the relationship to the proband was the weakest. In a regression analysis it did not add to the predictive model, and it did not change the predictive significance of the other variables. Thus, although this group had atypical familiarity with treatment options, this familiarity apparently did not distort the correlates of treatment-seeking behavior and therefore did little to limit generalizability.

As we have noted elsewhere [15], probands in the Collaborative Depression Study who began follow-up as they sought treatment at tertiary care centers were significantly more likely than matched comparison subjects without depression to experience a decline in income and occupational status over the ensuing 5 years. These differences were very robust. In contrast to proband intake, the recruitment of the subjects described here was not tied to treatment-seeking behavior. Within this group, the effect of untreated depression on long-term changes in occupational and income levels was present at only trend levels.

This underscores the range of severity encompassed by major depressive disorder. Probands had disorders that led them to seek help at tertiary care centers. Despite the fact that they sought help, their illness had marked effects on their socioeconomic status 5 years later. The untreated individuals described here had milder and shorter-lived illnesses and, despite the absence of treatment, did not show significant changes in socioeconomic status in the long term.

Individuals who had had untreated depression did report substantial psychosocial problems on follow-up. However, although these differences were robust for the likelihood of marital disruption and for ratings of interpersonal relationships and the enjoyment of activities (i.e., sexual satisfaction and recreational activities), measures of impairment in activities such as work, household duties, and frequency of sexual activity showed either no differences or differences that were much more modest. This pattern raises questions of cause and effect. Did dysfunction result from a depressive disorder, or did problematic interpersonal or cognitive styles give rise to both depressive symptoms and psychosocial difficulties?

The powerful effect of self-selection will make it very difficult to ever measure the value of treatment in mitigating the long-term psychosocial impact of major depressive disorder. Many subjects have participated in short-term, placebo-controlled treatment trials. Because such trials are extended in time, though, those who remain in the placebo or waiting-list

cells are increasingly biased toward those with naturally brief or mild conditions. Efficacy, dose finding, and blood level studies, particularly those which rely on advertisement for subject recruitment, may increase the likelihood of meaningful findings if they require durations and severity levels above those specified in most operational definitions of major depressive disorder.

ACKNOWLEDGMENTS

The National Institute of Mental Health Collaborative Program on the Psychobiology of Depression--Clinical Studies was conducted with the participation of the following investigators: M.B. Keller, M.D. (Chairperson, Providence); W. Coryell, M.D. (Co-Chairperson, Iowa City); H.S. Akiskal, M.D., J.D. Maser, Ph.D. (Washington, D.C.); P.W. Lavori, Ph.D., T.I. Mueller, M.D., M.T. Shea, Ph.D., M.G. Warshaw, M.S.S., M.A. (Providence); J. Fawcett, M.D., W.A. Scheftner, M.D. (Chicago); G. Winokur, M.D., J. Haley (Iowa City); J. Endicott, Ph.D., A. Leon, Ph.D., J. Loth, M.S.W. (New York); J. Rice, Ph.D., T. Reich, M.D. (St. Louis). Other contributors include N.C. Andreasen, M.D., Ph.D., P.J. Clayton, M.D., J. Croughan, M.D., G.L. Klerman, M.D. (deceased), R.M.A. Hirschfeld, M.D., M.M. Katz, Ph.D., E. Robins, M.D., R.W. Shapiro, M.D. (deceased), R.L. Spitzer, M.D., and M.A. Young, Ph.D.

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