Offspring of Depressed Parents

10 Years Later

Myrna M. Weissman, PhD; Virginia Warner, MPH; Priya Wickramaratne, PhD; Donna Moreau, MD; Mark Olfson, MD

Background: There have been numerous studies that have shown that offspring of depressed parents are at a high risk for major depressive disorder (MDD) and impairment. None have followed up the offspring into adulthood to obtain more precise estimates of risk.

Method: One hundred eighty-two offspring from 91 families, in which 1 or more parents had MDD (high risk) or in which neither parent was depressed (low risk), were blindly reassessed in the third follow-up, using a structured diagnostic instrument 10 years after their initial identification.

Results: Compared with the offspring for whom neither parent was depressed, the offspring of depressed parents had increased rates of MDD, particularly before puberty, and phobias (both at approximately a 3-fold risk), panic disorder, alcohol dependence (at a 5-fold risk), and greater social impairment. The peak age at onset for MDD in both high- and low-risk offspring ranged from 15 to 20 years. The peak age at onset for anxiety disorder was considerably earlier, especially in female offspring in the high-risk group. The onset of alcohol dependence in the offspring in the high-risk group peaked in adolescence and then after the age of 25 years. The depressed offspring of depressed parents, compared with nondepressed parents, had more serious and impairing depressions during the follow-up period but were *less* likely to go for treatment.

Conclusions: The offspring of depressed parents are a high-risk group for onset of anxiety disorder and MDD in childhood, MDD in adolescence, and alcohol dependence in adolescence and early adulthood. The findings support the potential value of early detection in the offspring of depressed parents.

Arch Gen Psychiatry. 1997;54:932-940

From the Department of Psychiatry, College of Physicians and Surgeons of Columbia University (Drs Weissman, Wickramaratne, Moreau, and Olfson), and Division of Clinical and Genetic Epidemiology, New York State Psychiatric Institute (Drs Weissman, Wickramaratne, and Olfson and Ms Warner), New York, NY.

MAJOR DEPRESSIVE disorder (MDD) is highly prevalent, impairing, and familial.[1,2] Recent studies have shown that the onset of MDD initially occurs in persons at an early age, often in the age range from their teens to 20s, although it can occur prepubertally, and the most familial form is that of an early onset before the age of 20 years.[3-7] Major depressive disorder most frequently affects women in their childbearing years.[5,8] Thus, study of their offspring has treatment and public health implications.[9] The increased risk of MDD in the offspring of depressed parents has been well documented. Although some of these studies have been criticized on methodological grounds (eg, small samples, cross-sectional design, absence of control groups, or assessment of both biological parents), they all have shown an increased rate of MDD in the offspring of depressed parents. Two short-term (ie, 18 months and 3 years) longitudinal offspring studies have shown an increased and continuing risk of MDD for offspring of depressed parents.[10-12]

There have also been longitudinal studies of depressed children or adolescents. These studies have not included assessment of parental psychiatric status and control groups, and with few exceptions, the studies have not followed up the children into adulthood.[13-20] Longitudinal studies of depressed children, even those that include assessment of family psychiatric history,[21] unlike high-risk studies, cannot provide age-specific rates of illness onset. To calculate rates of onset, the follow-up of cohorts of patients who are not ill at the time of subject ascertainment is required.

We have been following up a cohort of offspring, for whom either 1 or both parents have MDD or for whom neither parent has MDD. At the initial interview, we found that the offspring (age range, 6-23 years) of depressed, compared with nondepressed, parents had a significantly increased risk for MDD, anxiety disorders, and markedly poorer overall functioning.[22-26]

METHODS

SAMPLE

The offspring were initially selected for the presence or absence of a lifetime history of MDD based on Research Diagnostic Criteria in their parents.[22,23] The depressed probands had received treatment at the Yale University Depression Research Unit, New Haven, Conn. The normal control subjects came from a 1975 community survey that was conducted in New Haven, and they had no history of psychiatric illness, based on at least 4 direct interviews (the last 2 used the Schedule for Affective Disorders and Schizophrenia–Lifetime version[31] during a 10-year period). All probands were white and group-matched for age and sex.

At the initial interview (time 1), the sample consisted of 220 offspring between the ages of 6 and 23 years from 91 families, including 153 offspring from 65 families with 1 or more depressed parent and 67 offspring from 26 families with neither parent depressed.[22]

Two years after the initial interview (time 2), all 91 families were contacted for a second interview. Eighty-five (93%) of the 91 families consented to participate. Of the 220 offspring interviewed at time 1, 174 (79%) of them were reinterviewed at time 2.[26] An additional sample of 43 offspring who were not age-eligible at time 1 were interviewed also, but they are not described in the present study.

Ten years after the initiation of the study (time 10), families were recontacted for a reassessment. Among the 220 offspring interviewed at time 1, there were 2 deaths, and 1 offspring was found to have Down syndrome. Eighty-four percent (182/217) of those offspring who were interviewed at time 1 were reinterviewed at time 10. There were 4 deaths among the 91 probands who were eligible to be interviewed. Of the remaining 87 living probands, 73 (84%) were interviewed. Sixty-six spouses of probands were eligible to be interviewed. There were 5 deaths, and of the remaining 61 living spouses, 52 (85%) were interviewed. There were no deaths by suicide. There were no significant differences in the attrition rate of probands, spouses, or offspring by parental status.

Attrition for the probands and spouses did not vary significantly by sex or age. Attrition of offspring did not differ by sex. However, at time 10, older offspring were more likely to be interviewed than younger offspring (mean age, 28.5 vs 26.4 years; $t=-2.09$; $df=54.9$; $P=.04$). There were 2 first onsets of MDD (determined by use of the independent best estimate [BE] diagnosis that was made, blind to initial proband and offspring data) in the spouses in the nondepressed group between times 2 and 10. These 2 families had 4 offspring and were reassigned to the groups of depressed parents.

ASSESSMENT

Probands, spouses of probands, and offspring were independently interviewed with the Schedule for Affective Disorders and Schizophrenia–Lifetime version that was modified to include Research Diagnostic Criteria and *DSM-III* and *DSM-III-R* criteria.[32] All interviews of offspring were conducted blind to the parents' status and the offsprings' previous assessments. The interview covered a period of assessment from the last interview until the present and included the following additional data. Overall functioning was assessed by the interviewer on the Global Assessment Scale.[33] The Global Assessment Scale is scored on a scale from 0 to 100, with lower scores indicating impairment in overall functioning. Life charts were used to record all episodes of illness that occurred during the period of assessment. Adults completed the Social Adjustment Scale–Self-Report, which contained questions in major areas of functioning on a 4-point scale, with a higher score indicating more impairment.[34]

INTERVIEWERS

Interviewers (ie, PhD- and master's-level experienced mental health professionals) were located in Connecticut, where most of the subjects lived. The training of the interviewers took place during 4 group sessions (each session was 8 hours) and included supervised field interviews. Periodic interviews were monitored by the supervisor to limit interviewer drift. Interviewers participated in joint interviews in which 1 interviewer conducted the interview and the other corated the interview. A total of 80 cases were corated (in all possible pairs) by 4 interviewers at time 10. Using probable or definite *DSM-III-R* criteria, κ coefficients (SEs) were as follows: MDD, 0.78 (0.09); panic disorder, 0.79 (0.20); any anxiety, 0.65 (0.12); suicide attempts, 0.80 (0.11); alcohol abuse or dependence, 0.81 (0.09); drug abuse or dependence, 0.96 (0.03); and any psychiatric disorder, 0.80 (0.07).[35]

THE BE DIAGNOSIS

Diagnoses of offspring were based on the BE procedure.[36] To derive the BE diagnoses, an experienced clinician who was not involved in the interviewing, and who was blind to the diagnostic status of the parent and the previous assessments, independently reviewed all available information, including direct and informant interviews and medical records that were obtained at time 10, and assigned a *DSM-III-R* diagnosis for each offspring. A similar procedure was completed for parents who were independent and blind to offspring data. Six clinicians (3 psychiatrists, 2 psychologists, and 1 psychiatric nurse) with extensive diagnostic experience completed the BE diagnosis procedure. If there was disagreement, a consensus diagnosis was made. One hundred seventy-three cases across 3 samples using the same procedures and best estimators were reviewed independently by a second best estimator who was also blind. The number of cases for the second review was determined by calculating the number of cases necessary to have an 80% chance to detect a 0.2 difference between κ coefficients. Using probable or definite *DSM-III-R* criteria, κ coefficients (SEs) were as follows: MDD, 0.86 (0.03); panic disorder, 0.88 (0.11); any anxiety, 0.68 (0.06); suicidal behavior or attempts, 0.80 (0.07); alcohol abuse or dependence, 0.92 (0.03); drug abuse or dependence, 0.89 (0.03); any psychiatric disorder, 0.85 (0.04); and no history of mental illness, 0.80 (0.06).

The diagnoses used for this study were cumulative across times 1, 2, and 10. At times 1 and 2, *DSM-III* criteria were used. At time 10, *DSM-III-R* criteria was used. Impairment was considered to be a necessary criterion. Offspring were considered to be impaired if they sought treatment, took medication, were hospitalized, or had impaired functioning at work, school, or home.

DATA ANALYSIS

Sample differences in the means of continuous outcomes, by parental MDD, were tested by use of the *t* test and, for

Continued on next page

categorical outcomes, by use of the the χ^2 test. To test for the potential confounding effects of age and sex for continuous outcomes (ie, Social Adjustment Scale–Self-Report, number of days that person was depressed), a procedure for unbalanced analysis of covariance (Statistical Analysis System General Linear Model, SAS Institute Inc, Cary, NC)[37] was used to assess the means by parental MDD with the age and sex of the offspring in the model. The age and sex of the offspring were retained in the model if they were significant at the .05 level. Cross-sectional categorical data (eg, treatment, parental MDD) were examined by use of maximum likelihood logistic regressions (using the SAS LOGISTIC procedure), controlling for the age and sex of the offspring.[37] The antilogarithm of the regression coefficient for parental MDD yields an odds ratio (OR) for evaluating the magnitude of the association with parental MDD. Cumulative lifetime rates of disorder were computed in each of the 2 groups (at high and low risk) using standard methods of survival analysis.[38] These methods were adjusted for the fact that (1) the risk of disorder varied with the age of the offspring, (2) there was a wide variation in the ages of the offspring at the end of the follow-up period (age range, 16-34 years), and (3) the age distribution of the offspring in the 2 groups may have varied. A limitation of this method is that at the older ages, there may be relatively few offspring at risk; as a result, onsets of disorder at these ages may artificially inflate the estimates of cumulative survival rates. The equality of survival distributions for the offspring of depressed parents compared with that of the offspring of nondepressed parents was tested by means of the log rank test for homogeneity, which weighs greater survival times more heavily, and by means of the Wilcoxon test, which places more weight on early survival times. The age-specific incidence rates of psychiatric disorder were estimated in 5-year intervals using the lifetable method.[39] Where there were a sufficient number of cases of psychiatric disorder, the Cox multivariate proportional hazards model was used to assess the rates of psychiatric disorder by parental MDD with the age and sex of the offspring in the model.[40] The proportional hazards model applies the multiple regression method to a survival distribution and yields a ratio of the hazards of the outcome variables (ie, offspring diagnoses) for groups of interest (ie, parental MDD).

Two years later, the differences between the groups of offspring were more pronounced, with the offspring of depressed parents continuing to have an increased incidence of depression, high recurrence rates, and slower recovery.[27-29] Although there were few differences in symptom profiles among the depressed offspring by the clinical status of the parents, there were striking age-at-onset differences. All the prepubertal onsets occurred in the offspring of depressed parents who themselves had early onsets (age, <20 years).[24] There were no sex differences in the rates of prepubertal-onset MDD. After puberty, the female offspring showed a marked increase in onset of MDD that peaked between the ages of 15 and

Table 1. Demographic Characteristics of Probands (Parents) at Time 10 by Parental Diagnosis*

Characteristic	Parental Diagnosis: ≥1 With MDD (n=52)	Parental Diagnosis: Neither Had MDD (n=21)	Statistic†	*df*	*P*
Female, No. (%)	30 (58)	14 (67)	0.503	1	.47
Mean (SD) age, y	54.8 (8.3)	56.9 (6)	1.23	51.6	.22
Current marital status, No. (%)					
Single, never married	0	0	3.12	2	.21
Married, remarried	41 (79)	15 (75)			
Separated, divorced	9 (17)	2 (10)			
Widowed	2 (4)	3 (15)			
Current religion, No. (%)					
Protestant	11 (21)	5 (24)	2.95	3	.39
Catholic	34 (65)	14 (67)			
Jewish	2 (4)	2 (10)			
Other	5 (10)	0			
Employment status, No. (%)					
Full-time (≥35 h)	24 (46)	8 (38)	0.397	2	.82
Part-time (<35 h)	11 (21)	5 (24)			
Irregular, not employed	17 (33)	8 (38)			
Mean (SD) household income, $	49 801 (26 095)	59 393 (23 492)	1.45	36.5	.15

**Numbers may vary due to missing data. MDD indicates major depressive disorder.*

†† Statistic when the variable is continuous; χ^2 statistic when the variable is dichotomous.

20 years. For the male offspring, there was a gradual rise in onset after puberty.[29,30] The results also suggested that the depressed offspring of nondepressed parents have a different course of illness and that longer follow-up is required to capture clinically significant differences between the 2 groups.

The goal of the original study was to determine whether the lifetime rates of psychopathology (specifically MDD) in the offspring of depressed probands were greater than in the offspring of nondepressed parents. Comparisons were made in the overall lifetime rates of disorder (from birth to the time of interview) in the 2 groups. Because subjects were between the ages of 6 and 23 years, there was a wide variation in their stage of development at the first interview (time 1). As a consequence, many of the offspring at time 1 had not yet passed through the critical period of risk for the onset of depression, and the estimates of age-specific risks were unstable. With the availability of the 10-year follow-up, more precise estimates can be made of age-specific and cumulative lifetime rates.

RESULTS

CHARACTERISTICS OF PROBANDS AND OFFSPRING

At the 10-year follow-up, the depressed and nondepressed probands and their offspring did not differ by the major demographic variables, with 1 exception: the offspring of depressed compared with nondepressed par-

Table 2. Demographic Characteristics of Offspring at Time 10 by Parental Diagnosis*

Characteristic	Parental Diagnosis: ≥1 With MDD (n=129)	Parental Diagnosis: Neither Had MDD (n=53)	Statistic†	*df*	*P*
Female, No. (%)	71 (55.0)	29 (55)	0.002	1	.96
Age, No. (%)					
17-20 y	13 (10.1)	3 (6)	0.956	2	.62
21-28 y	56 (43.4)	25 (47)			
29-36 y	60 (46.5)	25 (47)			
Current marital status, No. (%)					
Single, never married	59 (46.8)	19 (36)	2.43	2	.29
Married, remarried	53 (42.1)	29 (55)			
Separated, divorced	14 (11.1)	5 (9)			
Ever divorced	14 (10.8)	7 (13)	0.204	1	.65
Current religion, No. (%)					
Protestant	27 (21.8)	7 (14)	4.90	3	.17
Catholic	72 (58.1)	38 (75)			
Jewish	4 (3.2)	2 (4)			
Other	21 (16.9)	4 (8)			
Educational level completed, No. (%)					
<High school	18 (13.9)	3 (6)	3.94	3	.26
High school only	48 (37.2)	21 (40)			
Some college or trade	23 (17.8)	14 (27)			
≥4 y college	40 (31.0)	14 (27)			
Employment status, No. (%)					
Full-time (≥35 h)	79 (61.7)	34 (64)	0.182	2	.91
Part-time (<35 h)	20 (15.6)	7 (13)	...	...	...
Irregular, not employed	29 (22.7)	12 (23)	...	...	...
Mean (SD) annual income, $					
Individual	22 759 (18 529)	26 179 (19 572)	1.06	86.1	.29
Household	49 214 (24 304)	54 158 (23 016)	1.18	96.4	.24
No. of children, mean (SD)	1.6 (0.79)	2.3 (1)	2.54	27.7	.02

*Numbers may vary due to missing data in some categories. MDD indicates major depressive disorder.
†t Statistic when the variable is continuous; χ^2 statistic when the variable is dichotomous.

ents had significantly *fewer children* (**Table 1** and **Table 2**).

CUMULATIVE RATES

During the 10-year follow-up, the offspring of depressed compared with nondepressed parents had higher rates of MDD and phobias (both at about 3-fold differences), panic disorder, and alcohol dependence (nearly a 5-fold difference) (**Table 3**). There was no significant interaction between parental depression status and parental and offspring gender for the risk of depression, anxiety, or alcohol dependence in offspring (data not given in Table 3).

AGE-SPECIFIC RATES

Figure 1 clearly shows that the peak time for the incidence period for both sexes for MDD was between the ages of 15 and 20 years. At all ages, the incidence by sex was higher in the offspring of depressed parents. There was a decline in the incidence after the age of 20 years. Prepubertal onset was uncommon and occurs in the high-risk offspring. The incidence rates were higher in female than male adolescents. After the age of 20 years, the incidence rates were similar in both sexes.

Figure 2 shows a different pattern for any anxiety disorder (including panic disorder, generalized anxiety disorder, agoraphobia, social phobia, simple phobia, separation anxiety, obsessive-compulsive disorder, and overanxious disorder). The peak incidence of anxiety in the offspring for both sexes was much earlier than that for MDD (age range, 5-10 years), especially in the offspring of depressed parents. Anxiety disorders that have an early onset are mostly phobias and separation anxiety disorder (mean ages at onset, 5.2 and 6.6 years, respectively). The incidence rates decline after the age of 12 years and converge by the sex of the offspring and parental diagnosis.

The incidence rate for alcohol dependence in both sexes of depressed probands increased at the ages of 15 to 20 years and after the age of 25 years (**Figure 3**).

SYMPTOMS OF DEPRESSION

Symptom patterns of depression (not shown) by the age at first onset (age, <14 and ≥14 years) in the offspring at time 10 showed only 1 significant difference (from a list of 27 symptoms) (χ^2=7.78; *df*=1; *P*=.005). These analyses were rerun by comparing symptom patterns in persons with onsets that occurred at younger than 18 years with symptom patterns that occurred in persons with onsets at age 18 years and older, and the results were similar. There were few differences in depressive symptoms in the offspring by

Table 3. Cumulative Rates of Disorder (Using *DSM-III-R*) (Applying Impairment Criteria) in Offspring by Parental Diagnosis*

Diagnoses in Offspring	Parental Diagnosis, No. (%) of Offspring: ≥1 With MDD (n=129)	Parental Diagnosis, No. (%) of Offspring: Neither Had MDD (n=53)	Relative Risk† (95% Confidence Interval)
Any mood disorder	87 (85.3)	20 (38)	2.39 (1.46-3.89)
MDD	64 (56.4)	13 (25)	2.50 (1.38-4.54)
Bipolar	3 (2.3)	0	. . .‡
Dysthymia	7 (6.1)	3 (6)	0.922 (0.238-3.58)
Any anxiety	51 (41.7)	8 (15)	2.96 (1.41-6.24)
Phobias	27 (21.0)	4 (8)	2.94 (1.03-8.41)
Panic disorder	14 (13.4)	0	. . .§
OCD	1 (1.9)	1 (2)	. . .‖
GAD	0	0	
ADHD	5 (3.9)	2 (4)	0.882 (0.166-4.67)
Any substance abuse	40 (32.0)	14 (28)	1.32 (0.715-2.42)
Alcohol abuse	18 (14.5)	8 (16)	0.934 (0.406-2.15)
Alcohol dependence	21 (21.6)	2 (7)	4.93 (1.16-21.06)
Drug abuse	7 (5.5)	7 (14)	0.414 (0.145-1.18)
Drug dependence	16 (14.5)	1 (2)	6.98 (0.925-52.74)
Schizophrenia	2 (1.8)	0	. . .¶
Childhood disorders			
Separation anxiety	16 (12.4)	6 (11)	1.08 (0.424-2.78)
Conduct disorder	44 (34.1)	11 (21)	1.88 (0.969-3.64)#
Overanxious disorder	17 (13.6)	1 (2)	7.22 (0.959-54.28)
Any of the previously cited diagnoses	99 (78.4)	25 (47)	2.18 (1.40-3.38)

**If the offspring reported (in the Schedule for Affective Disorders and Schizophrenia), during an episode of disorder, that they sought help, took medication, were hospitalized, or had impaired functioning at work, school, or home, they were considered to be impaired. MDD indicates major depressive disorder; OCD, obsessive-compulsive disorder; GAD, generalized anxiety disorder; and ADHD, attention deficit hyperactivity disorder.*

†Relative risk adjusted for age and sex of offspring.

‡Two-tailed Fisher exact test=1.25, df=1, P=.56.

§Two-tailed Fisher exact test=6.23, df=1, P=.004.

‖Two-tailed Fisher exact test=0.427, df=1, P>.99.

¶Two-tailed Fisher exact test=0.831, df=1, P>.99.

#Data on impairment were not collected for conduct disorder.

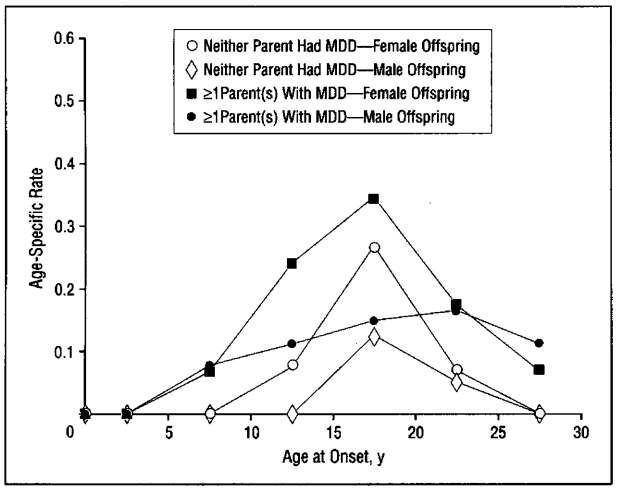

Figure 1. *Age-specific rates of major depressive disorder (MDD) by parental MDD and sex of offspring (N=182 [lifetime]).*

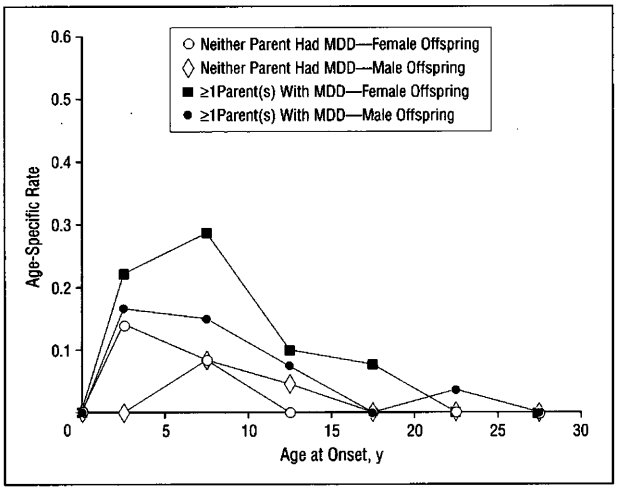

Figure 2. *Age-specific rates of any anxiety disorder by parental major depressive disorder (MDD) and sex of offspring (N=182 [lifetime]).*

proband group. Of 27 symptoms, the offspring of depressed parents more frequently reported feelings of worthlessness (χ^2=3.86; *df*=1; *P*=.05), and the offspring of nondepressed parents more frequently reported a loss of interest in sex (χ^2=7.63; *df*=1; *P*=.006). The significant differences that were found could have been due to chance because of the large number of comparisons made.

COMORBIDITY

Comorbidity of other disorders with MDD was high in the offspring from both groups (**Table 4**). While the stratified ORs suggest that there are higher rates of comorbidity in the offspring of *nondepressed* parents, our small sample size does not give adequate power to test whether the ORs differ significantly. Using the Breslow-

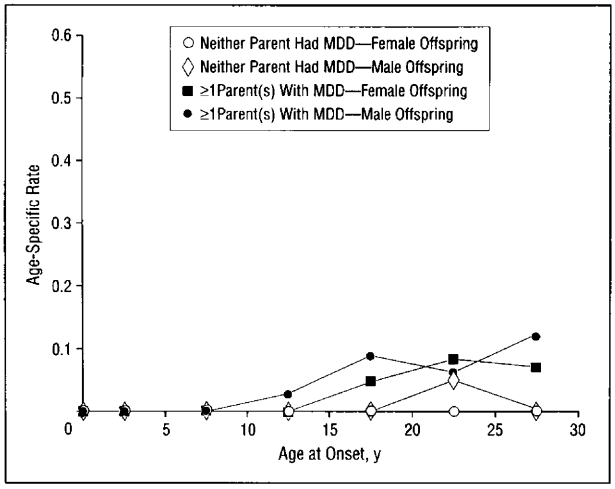

Figure 3. *Age-specific rates of alcohol dependence by parental major depressive disorder (MDD) and sex of offspring (N=182 [lifetime]).*

Day test for homogeneity of the ORs, there was only a suggestion that the ORs for comorbidity of dysthymia (χ^2=2.61; *df*=1; *P*=.11), any drug abuse or dependence (χ^2=1.88; *df*=1; *P*=.17), any phobias (χ^2=2.43; *df*=1; *P*=.12), and any of the previously described diagnoses with MDD (χ^2=2.40; *df*=1; *P*=.12) were higher in the offspring of nondepressed parents.

TREATMENT AND IMPAIRMENT

Throughout the 10 years, the offspring of depressed compared with nondepressed parents received slightly more outpatient treatment, and they had poorer overall functioning, as well as poorer functioning in work, family, and marriage (**Table 5**).

SEVERITY OF OUTCOME IN DEPRESSED OFFSPRING

Table 6 takes into account the depression status of the offspring and shows that the illness severity at time 10, in the offspring who were depressed at time 1 or 2, was greater in the offspring of depressed compared with nondepressed parents. The depressed offspring of depressed parents were *less* likely to go for treatment when they felt that they needed it, and *less* likely to receive treatment when they were depressed. More than 30% of the depressed offspring of depressed parents never received any treatment. They also had more impairment overall, in work and marriage, and more days on which they felt depressed.

COMMENT

Like previous investigators, we found that parental depression increases the risk of offspring depression, that the course of depression in children (as in adults) is protracted, that the morbidity rate is high, and that the overall symptom picture in offspring does not vary by the age at onset of the symptoms and does not differ by proband group.[11,12,15,16,41,42]

The overall rates and burden of illness are greater in the offspring of depressed parents, and their offspring continue to have higher rates of MDD (ie, a 3-fold increase) and anxiety disorders. As they mature, they also have high rates of alcohol dependence (ie, 5-fold increases) and poorer functioning in work, family, and marriage. The cumulative rate of MDD in the offspring of nondepressed parents (25.1/100) for the ages of 6 to 36 years is higher than that in the community sample for the ages of 15 to 34 years (17.1/100),[5,6] and it may be explained by our closer surveillance of the sample (ie, 3 interviews), as well as by their younger ages when the interviewing began.

The recurrent nature of depression that was found is consistent with findings from longitudinal studies of depressed adults and children.[16,17,43,44] The increased risk of MDD in the offspring of depressed parents is consistent with that found in numerous studies in which the offspring were minors.[9,11,44,45] The familial nature of depression was consistent with that of studies in which the probands were depressed children or adults.[21,46,47] While the absolute rates vary with the design and criteria used, the magnitude of the effect of familial depression (ie, a 2- to 3-fold increased risk) is consistent across high-risk and family studies.

There were more shifts to bipolar disorders in the offspring of depressed than nondepressed parents, but the overall rate of bipolar disorder (2.3% in the off-

Table 4. Comorbidity of Offspring MDD With Other *DSM-III-R* Diagnoses by Parental Diagnosis (Cumulative Rates for Times 1, 2, and 10)*

Parental Diagnosis	MDD in Offspring, No. (%)		Odds Ratio (95% Confidence Interval)
	No	Yes	
≥1 Parent(s) depressed	60 (100)	69 (100)	
Any anxiety	17 (28)	43 (62)	4.18 (2.02-8.67)
Dysthymia	12 (20)	26 (38)	2.42 (1.09-5.33)
Any phobia	5 (8)	22 (32)	5.14 (1.92-13.76)
Any alcohol abuse	9 (15)	23 (33)	2.83 (1.21-6.64)
Panic disorder	2 (3)	13 (19)	6.73 (1.71-26.46)
OCD	0	3 (4)	. . .†
Any drug abuse	9 (15)	14 (20)	1.44 (0.57-3.62)
Any substance abuse	12 (20)	28 (41)	2.73 (1.24-5.98)
Any of the previously cited diagnoses	30 (50)	57 (83)	4.75 (2.18-10.33)
Neither parent depressed	39 (100)	14 (100)	
Any anxiety	3 (8)	6 (43)	9.00 (2.11-38.22)
Dysthymia	5 (13)	8 (57)	9.07 (2.42-33.91)
Any phobia	0	4 (29)	. . .‡
Any alcohol abuse	6 (15)	6 (43)	4.12 (1.09-15.61)
Panic disorder	0	0	
OCD	0	1 (7)	. . .§
Any drug abuse	4 (10)	5 (36)	4.86 (1.15-20.47)
Any substance abuse	9 (23)	8 (57)	4.44 (1.26-15.66)
Any of the previously cited diagnoses	13 (33)	13 (93)	26.00 (4.81-140.47)

**MDD indicates major depressive disorder; OCD, obsessive-compulsive disorder.*
†Two-tailed Fisher exact test=2.67, df=*1,* P=*.25.*
‡Two-tailed Fisher exact test=12.05, df=*1,* P=*.03.*
§Two-tailed Fisher exact test=2.84, df=*1,* P=*.26.*

Table 5. Treatment, Work Impairment, and Overall Functioning in Offspring by Parental Diagnosis*

Parameter	Parental Diagnosis: ≥1 With MDD (n=129)	Parental Diagnosis: Neither Had MDD (n=53)	Odds Ratio† (95% Confidence Interval)	F	df	P
Lifetime treatment for emotional problems, No. (%)						
Outpatient treatment	67 (52)	18 (34)	2.11 (1.08-4.11)	...	...	...
Hospitalization	8 (6)	3 (6)	1.09 (0.280-4.32)	...	...	...
Ever out of work in last 5 y due to psychopathologic disorder, No. (%)	13 (10)	1 (2)	6.50 (0.820-51.62)	...	...	...
Overall functioning (Global Assessment Scale score, ≤71), No. (%)	42 (33)	6 (11)	3.78 (1.50-9.56)	...	...	...
Social Adjustment Scale, mean (SD) score‡						
Work	1.80 (1.1)	1.45 (0.63)	...	4.50	1	.04
Social and leisure	1.97 (0.52)	1.81 (0.41)	...	3.47	1	.06
Extended family	1.66 (0.48)	1.45 (0.35)	...	8.05	1	.005
Marital	1.89 (0.58)	1.53 (0.35)	...	8.16	1	.005
Parental	1.44 (0.39)	1.26 (0.42)	...	1.94	1	.17
Family	1.75 (0.58)	1.73 (0.63)	...	0.03	1	.85
Overall	1.79 (0.42)	1.59 (0.33)	...	8.88	1	.003

*Numbers may vary due to missing data. MDD indicates major depressive disorder.
†Odds ratio adjusted for age and sex of offspring.
‡Means adjusted for age of offspring.

Table 6. Severity of Outcome at Time 10 in Offspring With Any Depression at Time 1 or 2 by Parental Diagnosis*

Parameter	Parental Diagnosis: ≥1 With MDD (n=80)	Parental Diagnosis: Neither Had MDD (n=26)	Odds Ratio (95% Confidence Interval)†	Statistic‡	df	P
Did not go for treatment when felt it was needed, No. (%)	23 (33)	1 (4)	12.85 (1.61-102.54)	...	...	...
Global Assessment Scale score, ≤71, No. (%)	32 (40)	4 (15)	4.34 (1.33-14.14)	...	...	...
Social Adjustment Scale, mean (SD) score						
Work	1.84 (1.07)	1.30 (0.324)	...	−3.66	88.5	<.001
Social and leisure	1.97 (0.567)	1.89 (0.450)	...	−0.689	49	.49
Extended family	1.68 (0.509)	1.46 (0.314)	...	−2.54	64.6	.01
Marital	1.88 (0.630)	1.47 (0.358)	...	−3.05	46.1	.003
Parental	1.44 (0.402)	1.22 (0.405)	...	−1.44	23.2	.16
Family	1.78 (0.601)	1.61 (0.502)	...	−1.37	44.3	.18
Overall	1.80 (0.455)	1.59 (0.332)	...	−2.56	55.2	.01
No. of days depressed during follow-up, mean (SD)	118 (401)	11 (49)	...	−2.33	86	.02
Ever out of work in last 5 y due to psychopathologic disorder, No. (%)	11 (14)	1 (4)	...	1.92	1	.29§
No. of MDD episodes during follow-up, No. (%)						
0	53 (66)	23 (88)	...	...	...	...
1	23 (29)	2 (8)	...	...	...	...
2+	4 (5)	1 (4)	...	5.10	2	.08
Suicidal gestures or attempts, No. (%)	13 (16)	3 (12)	...	0.340	1	.75§
Treatment during 10 y, No. (%)‖						
Outpatient treatment	33 (67)	6 (100)	...	2.76	1	.16§
Hospitalization	4 (8)	3 (50)	...	8.42	1	.02§
Any treatment	33 (67)	6 (100)	...	2.76	1	.16§

*Numbers may vary due to missing data. Odds ratios that were adjusted for age and sex of offspring (95% confidence interval) were as follows: offspring who did not go for treatment, 12.85 (1.61-102.54); Global Assessment Scale score, 4.34 (1.33-14.14). MDD indicates major depressive disorder.
†Adjusted for age and sex of offspring.
‡†Statistic is used for continuous variables; χ^2 statistic is used for dichotomous.
§Two-tailed Fisher exact test.
‖Treatment of MDD for offspring with any depression at time 10: 1 or more parent(s) with MDD (n=49) and neither parent had MDD (n=6).

spring of depressed parents) was lower than that reported by other investigators.[15,16] Of note, some of the offspring have not fully passed through the age at risk for the onset of bipolar disorder.

A prepubertal onset of MDD is uncommon, and it did not occur in the offspring of the nondepressed parents. The peak first onset of MDD in middle and late adolescence is consistent with the findings from epidemio-

logic studies of adolescents and adults.[3,6,45,48,49] This peak is consistent in female offspring regardless of proband diagnosis, suggesting a consistent vulnerability period for focus on detection and intervention. Why the rates should increase so abruptly in young females in middle and late adolescence and early adulthood is still unclear and is an area for further research. Parental affective disorders further increase the risk of first onset in adolescents. However, as noted by Beardslee et al,[45] affective disorders in parents may serve as an identifier of a constellation of risk factors. Symptoms by themselves do not discriminate risks.[45] Studies of the phenomenology of depressive disorders across childhood and adulthood have generally found similar symptoms across the ages.[20,42,50,51] The finding that anxiety disorder precedes the onset of MDD and is markedly increased in the offspring of depressed parents may be due to high rates of comorbid anxiety disorders in the parents. Alternately, early expression of anxiety disorders could constitute an underlying vulnerability to psychopathology by shared genetic or environmental factors.[52] Our analysis of sibling resemblance for MDD, anxiety, and conduct disorder at time 1 found that sibling resemblance in the high-risk cohort was substantially greater than in the low-risk cohort for anxiety disorders but not MDD, suggesting that anxiety disorders may reflect the most pronounced familial influences common to siblings at high risk for MDD.[53]

While, to our knowledge, this is the largest published offspring study of depressed parents and has the longest follow-up period, our sample of offspring with a broad age range is still small, and there were few offspring with a prepubertal onset of depression. The selection of parents from treatment settings may have resulted in more serious cases.[54] On the other hand, the similarity of findings from several studies that used different methods suggests the validity of the findings.

The current findings support initiatives aimed at early detection and possible treatment intervention in the parents of depressed offspring and the offspring of depressed parents. Physicians who specialize in pediatrics and adolescent medicine, as well as internists, family physicians, and child psychiatrists, are particularly well positioned to inquire about the mental health history of their patient's parents.[55]

Alternately, psychiatrists who treat adult patients should inquire about the clinical status of the offspring. Successful treatment of parental depression may provide primary prevention by reducing the symptoms of depression that may impair parenting.[56] A recent study suggested that depressed mothers who give negative self-reports may be more negative than their directly observed parenting behavior.[57] However, women who were chronically or severely depressed had both negative self-reports and observed negative parent-child relationships, suggesting that this is a particularly high-risk group for intervention. Secondary prevention may be achieved through the early detection and treatment of high-risk offspring who exhibit early or minor forms of anxiety, depressive, or substance abuse disorders. Finally, the aggressive treatment of established MDD (ie, tertiary prevention) may reduce the high level of social impairment that characterizes the depressed offspring of depressed parents.

Only a small proportion of young people with mental disorders receive adequate mental health treatment.[58-60] In the current study, a large number of the offspring who perceived a need for mental health care utilized no treatment whatsoever. One possible explanation is that the offspring of depressed parents develop negative attitudes toward mental health treatment because they associate it with their parents' chronic course of illness. Alternately, the depressed parent may deny that their offspring have the same disorder. A better understanding of how parental factors influence the seeking of health care for their offspring may help public health planners extend treatment to this vulnerable and underserved population.[61]

There are now strong financial incentives to limit treatment, and the assessment of clinical outcomes focuses on short-term treatment costs.[62] Our data suggest that outcomes should assess the impact of parental depression on the offspring over time.

Accepted for publication January 28, 1997.

This work was supported in part by grants MH-36197 (Dr Weissman) and 5P30MH43878 (Dr Weissman), and by Research Scientist Development Award K20-MH01042 (Dr Olfson) from the National Institute of Mental Health, Rockville, Md.

Corresponding author: Myrna M. Weissman, PhD, College of Physicians and Surgeons of Columbia University, New York State Psychiatric Institute, 722 W 168th St, New York, NY 10032 (e-mail: weissman@child.cpmc.columbia.edu).

REFERENCES

1. Klerman GL, Weissman MM. Increasing rates of depression. *JAMA.* 1989;261:2229-2235.
2. Weissman MM, Klerman GL. Depression: current understanding and changing trends. *Annu Rev Public Health.* 1992;13:319-339.
3. Christie KA, Burke JD, Regier DA, Rae DS, Boyd JH, Locke BZ. Epidemiologic evidence for early onset of mental disorders and higher risk of drug abuse in young adults. *Am J Psychiatry.* 1988;145:971-975.
4. Lahey BB, Flagg EW, Bird HR, Schwab-Stone M, Canino G, Dulcan MK, Leaf PJ, Davies M, Bourdon K, Horwitz S, Rubio-Stipec M, Freeman DH, Shaffer D, Goodman SH, Narrow WE, Weissman MM, Kandel D, Jensen PS, Richters JE, Regier DA. The NIMH Methods for the Epidemiology of Children and Adolescents (MECA) Study: background and methodology. *J Am Acad Child Adolesc Psychiatry.* 1996;35:855-864.
5. Kessler RC, McGonagle KA, Nelson CB, Hughes M, Swartz M, Blazer DG. Sex and depression in the National Comorbidity Survey, II: cohort effects. *J Affect Disord.* 1994;30:15-26.
6. Kessler RC, McGonagle KA, Shanyang Z, Nelson CB, Hughes M, Eshleman S, Wittchen HU, Kendler KS. Lifetime and 12-month prevalence of *DSM-III-R* psychiatric disorders in the United States. *Arch Gen Psychiatry.* 1994;51:8-19.
7. Weissman MM, Gershon ES, Kidd KK, Prusoff BA, Leckrnan JF, Dibble E, Harnovit J, Thompson WD, Pauls DL, Guroff JJ. Psychiatric disorders in the relatives of probands with affective disorders: the Yale University–National Institute of Mental Health Collaborative Study. *Arch Gen Psychiatry.* 1984;41:13-21.
8. Weissman MM, Olfson M. Depression in women: implications for health care research. *Science.* 1995;269:799-801.
9. Beardslee WR, Keller MB, Klerman GL. Children of parents with affective disorder. *Int J Fam Psychiatry.* 1985;6:283-299.
10. Orvaschel H, Walsh-Allis G, Ye W. Psychopathology in children of parents with recurrent depression. *J Abnorm Child Psychol.* 1988;16:17-28.
11. Hammen C, Burge D, Burney E, Adrian C. Longitudinal study of diagnoses in children of women with unipolar and bipolar affective disorder. *Arch Gen Psychiatry.* 1990;47:1112-1117.
12. Hammen C, Burge D, Adrian C. Timing of mother and child depression in a longitudinal study of children at risk. *J Consult Clin Psychol.* 1991;59:341-345.
13. Lewinsohn PM, Gotlib IH, Seeley JR. Adolescent psychopathology, IV: specificity of psychosocial risk factors for depression and substance abuse in older adolescents. *J Am Acad Child Adolesc Psychiatry.* 1995;34:1221-1229.

14. Rao U, Weissman MM, Martin JA, Hammond RW. Childhood depression and risk of suicide: a preliminary report of a longitudinal study. *J Am Acad Child Adolesc Psychiatry.* 1993;32:21-27.
15. Rao U, Ryan ND, Birmaher B, Dahl RE, Williamson DE, Kaufman J, Rao R, Nelson B. Unipolar depression in adolescents: clinical outcome in adulthood. *J Am Acad Child Adolesc Psychiatry.* 1995;34:566-577.
16. Kovacs M, Feinberg TL, Crouse-Novak MA, Paulauskas SL, Finkelstein R. Depressive disorders in childhood, I: a longitudinal prospective study of characteristics and recovery. *Arch Gen Psychiatry.* 1984;41:229-237.
17. Kovacs M, Goldston D, Gatsonis C. Suicidal behaviors and childhood-onset depressive disorders: a longitudinal investigation. *J Am Acad Child Adolesc Psychiatry.* 1993;32:8-20.
18. Ferdinand RF, Verhulst FC. Psychopathology from adolescence into young adulthood: an 8-year follow-up study. *Am J Psychiatry.* 1995;152:1586-1594.
19. Orvaschel H, Lewinsohn PM, Seeley JR. Continuity of psychopathology in a community sample of adolescents. *J Am Acad Child Adolesc Psychiatry.* 1995;34:1525-1535.
20. Harrington R, Fudge H, Rutter M, Pickles A, Hill J. Adult outcomes of childhood and adolescent depression, I: psychiatric status. *Arch Gen Psychiatry.* 1990;47:465-473.
21. Harrington RC, Fudge H, Rutter ML, Bredenkamp CG, Pridham J. Child and adult depression: a test of continuities with data from a family study. *Br J Psychiatry.* 1993;162:627-633.
22. Weissman MM, John K, Merikangas KR, Prusoff BA, Wickramaratne P, Gammon GD, Angold A, Warner V. Depressed parents and their children: general health, social and psychiatric problems. *AJDC.* 1986;140:801-805.
23. Weissman MM, Gammon GD, John K, Merikangas KR, Warner V, Prusoff BA, Sholomskas D. Children of depressed parents: increased psychopathology and early onset of major depression. *Arch Gen Psychiatry.* 1987;44:847-853.
24. Weissman MM, Warner V, Wickramaratne P, Prusoff BA. Early onset major depression in parents and their children. *J Affect Disord.* 1988;15:269-278.
25. Chang G, Weissman MM, Warner V. Physicians' recognition of psychiatric disorders in children and adolescents. *AJDC.* 1988;142:736-739.
26. Fendrich M, Warner V, Weissman MM. Family risk factors, parental depression and childhood psychopathology. *Dev Psychol.* 1990;26:40-50.
27. Warner V, Weissman MM, Fendrich M, Wickramaratne PJ, Moreau D. The course of major depression in the offspring of depressed parents: incidence, recurrence, recovery. *Arch Gen Psychiatry.* 1992;49:797-801.
28. Weissman MM, Fendrich M, Warner V, Wickramaratne PJ. Incidence of psychiatric disorder in offspring at high and low risk for depression. *J Am Acad Child Adolesc Psychiatry.* 1992;31:640-648.
29. Fendrich M, Weissman MM, Warner V. Longitudinal assessment of major depression and anxiety disorders in children. *J Am Acad Child Adolesc Psychiatry.* 1991;30:67-74.
30. Fendrich M, Weissman MM, Warner V, Mufson L. Two-year recall of lifetime diagnoses in offspring at high and low risk for major depression: the stability of offspring reports. *Arch Gen Psychiatry.* 1990;47:1121-1127.
31. Endicott J, Spitzer RL. A diagnostic interview: the Schedule for Affective Disorders and Schizophrenia. *Arch Gen Psychiatry.* 1978;35:837-844.
32. Mannuzza S, Fyer AJ, Klein DF, Endicott J. Schedule for Affective Disorders and Schizophrenia–Lifetime version modified for the study of anxiety disorders (SADS-LA): rationale and conceptual development. *J Psychiatr Res.* 1986;20:317-325.
33. Endicott J, Spitzer RL, Fleiss JL, Cohen J. The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry.* 1976;33:766-771.
34. Weissman MM, Bothwell S. The assessment of social adjustment by patient self-report. *Arch Gen Psychiatry.* 1976;33:1111-1115.
35. Cohen JA. A coefficient of agreement for nominal scales. *Educ Psychol.* 1960;20:37-46.
36. Leckman JF, Sholomskas D, Thompson D, Belanger A, Weissman MM. Best estimate of lifetime psychiatric diagnosis: a methodological study. *Arch Gen Psychiatry.* 1982;39:879-883.
37. SAS Institute Inc. *SAS/STAT User's Guide: Version 6.* 4th ed. Cary, NC: SAS Institute Inc; 1990:2.
38. Cox DR, Oakes D. *Analysis of Survival Data.* New York, NY: Chapman & Hall; 1984.
39. Kalbfeisch JD, Prentice RL. *The Statistical Analysis of Failure Time Data.* New York, NY: John Wiley & Sons Inc; 1980.
40. Cox DR. Regression models and life tables. *J R Stat Soc Ser B.* 1972;34:187-220.
41. Lewinsohn PM, Hoberman HM, Rosenbaum M. A prospective study of risk factors for unipolar depression. *J Abnorm Psychol.* 1988;97:251-264.
42. Ryan ND, Puig-Antich J, Ambrosini P, Rabinovich H, Robinson D, Nelson B, Lyengar S, Twomey J. The clinical picture of major depression in children and adolescents. *Arch Gen Psychiatry.* 1987;44:854-861.
43. Lavori PW, Keller MB, Mueller TI, Scheftner W, Fawcett J, Corvell W. Recurrence after recovery in unipolar MDD: an observational follow-up study of clinical predictors and somatic treatment as a mediating factor. *Int J Methods Psychiatr Res.* 1994;4:211-229.
44. Keller MB, Beardslee WR, Dorer DJ, Lavori PW, Samuelson H, Klerman GL. Impact of severity and chronicity of parental affective illness on adaptive functioning and psychopathology in children. *Arch Gen Psychiatry.* 1986;43:930-937.
45. Beardslee WR, Keller MB, Seifer R, Lavori PW, Staley J, Podoresfsky D, Shera D. Prediction of adolescent affective disorder: effects of prior parental affective disorders and child psychopathology. *J Am Acad Child Adolesc Psychiatry.* 1996;35:279-288.
46. Weissman MM, Wickramaratne P, Merikangas KR, Leckman JF, Prusoff BA, Caruso KA, Kidd KK, Gammon GD. Onset of major depression in early adulthood: increased familial loading and specificity. *Arch Gen Psychiatry.* 1984;41:1136-1143.
47. Williamson DE, Ryan ND, Birmaher B, Dahl RE, Kaufman J, Rao U, Puig-Antich J. A case-control family history study of depression in adolescents. *J Am Acad Child Adolesc Psychiatry.* 1995;34:1596-1607.
48. Angold A. Childhood and adolescent depression, I: epidemiological and aetiological aspects. *Br J Psychiatry.* 1988;152:601-617.
49. Fleming J, Offord DR, Boyle MH. Prevalence of childhood and adolescent depression in the community: Ontario Child Health Study. *Br J Psychiatry.* 1989;155:647-654.
50. Carlson GA, Kashani JH. Phenomenology of major depression from childhood through adulthood: analysis of three studies. *Am J Psychiatry.* 1988;145:1222-1225.
51. Roberts RE, Lewinsohn PM, Seeley JR. Symptoms of *DSM-III-R* major depression in adolescence: evidence from an epidemiological survey. *J Am Acad Child Adolesc Psychiatry.* 1995;34:1608-1617.
52. Merikangas KR. Genetic epidemiologic studies of affective disorders in childhood and adolescence. *Eur Arch Psychiatry Clin Neurosci.* 1993;243:121-130.
53. Rende R, Wickramaratne P, Warner V, Weissman MM. Sibling resemblance for psychiatric disorders in offspring at high and low risk for depression. *J Child Psychol Psychiatry.* 1995;36:1353-1363.
54. Kendler K. Is seeking treatment for depression predicted by a history of depression in relatives? implications for family studies of affective disorder. *Psychol Med.* 1995;25:807-814.
55. Takeuchi DT, Bui KV, Kin L. The referral of minority adolescents to community mental health centers. *J Health Soc Behav.* 1993;34:153-164.
56. Weissman MM, Paykel ES, Klerman GL. The depressed woman as a mother. *Soc Psychiatry Psychiatr Epidemiol.* 1982;7:98-108.
57. Frankel KA, Harmon RJ. Depressed mothers: they don't always look as bad as they feel. *J Am Acad Child Adolesc Psychiatry.* 1996;35:289-298.
58. Keller MB, Lavori PW, Beardslee WR, Wunder J, Ryan N. Depression in children and adolescents: new data on 'undertreatment' and a literature review on the efficacy of available treatments. *J Affect Disord.* 1991;21:163-171.
59. Burns BJ. Mental health services use by adolescents in the 1970s and 1980s. *J Am Acad Child Adolesc Psychiatry.* 1991;30:144-150.
60. Bird HR, Canino G, Rubio-Stipec M, Gould MS, Ribera J, Sesman M, Woodbury M, Hertas-Goldman S, Pagan A, Sanchez-Lacay A, Moscoso M. Estimates of the prevalence of childhood maladjustment in a community survey in the relevance of childhood maladjustment in a community survey in Puerto Rico: the use of combined measures. *Arch Gen Psychiatry.* 1988;45:1120-1126.
61. Leaf PJ, Bruce ML, Tischler GL. The differential effect of attitudes on the use of mental health services. *Soc Psychiatry Psychiatr Epidemiol.* 1986;21:187-192.
62. Schowalter JE. Managed care: income to outcome. *J Am Acad Child Adolesc Psychiatry.* 1995;34:1123.