

# Parental Depression Risk: Comparing Youth with Depression, Attention Deficit Hyperactivity Disorder and Community Controls

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## Abstract

**Objective:** Family studies of youth with depression are reviewed and new data presented. Past studies suggest strong familiarity of youth depression. However, few studies included direct interviews with fathers and both psychiatric and normal control groups. In this study, lifetime prevalences of parental Major Depressive Disorder (MDD), Recurrent Depression, Dysthymic Disorder (DD), Double Depression (MDD/DD) and Bipolar Disorder were compared for 6-18 year old youth with depression (n = 127), youth with ADHD without a depression history (n = 116), and community control youth (n = 78).

**Method:** Parental diagnoses were made by diagnosticians blind to child diagnostic status using best estimate procedures based on the parent-interview SADS and the Family History Interview of Psychiatric Status from the other parent. Child diagnoses were based on K-SADS interviews conducted with both parent and child separately.

**Results:** Both mothers and fathers of depressed probands were significantly more likely than mothers and fathers of the other proband groups to have a history of MDD and DD. Mothers of probands with MDD/DD had higher rates of MDD compared to mothers of other depressed probands. There were few cases of parental Bipolar Disorder and most occurred in parents of probands with depression.

**Conclusion:** The current findings provide further evidence of the strong familiarity of youth depression and highlight the need to evaluate parents when treating depressed youth. A comprehensive treatment approach may need to include a focus on obtaining treatment for and enhancing coping with parental depression.

**Keywords:** Depression; Bipolar disorder; Mood disorders; Youth; Family; Genetics; Familial risk; Parental depression

## Introduction

The contribution of genetic factors to the etiology of depression in adults is well established, with heritability for major depressive disorder estimated at about 39% [1]. Compared to relatives of normal controls, relatives of adults with depression show increased rates of lifetime mood disorders [2-4]. There are also generally consistent findings indicating that bipolar disorder tends to run in families of bipolar probands; whereas, unipolar depression runs in families of both bipolar and unipolar probands [2,4,5]. Studies of family aggregation provide opportunities to examine vulnerability factors and mechanisms, better understand heterogeneity in diagnostic presentation, and uncover familial phenotypes [6]. Examination of family aggregation in youth may also provide important information on continuities between adult and youth depressive disorders [6-8]. Additionally, identification of biological subtypes provides potential opportunities for prevention of poor outcomes through increased attention to environmental factors that interact with this risk [9].

## Top-down studies of family aggregation

A number of studies have used a “top-down” or “high risk” approach to examining the familiarity of mood disorders – selecting adult depressed and/or bipolar probands and assessing the risk of mood disorders in their offspring. These top-down studies provide strong evidence that parental depression is associated with higher risk for both depressive symptoms and disorders in offspring [10], with youth of depressed parents estimated to be 4 times as likely to experience a major depressive episode compared to those without a history of parental depression [6]. Given gender differences in rates

of depression and the greater availability of mothers than fathers to participate in research, most studies of depression in families have focused on maternal depression [11]. These studies indicate higher rates of diagnosis, recurrence, and chronicity of depression among offspring of depressed parents compared to those without depressed parents [6,12,13]. Even remitted parental depression may be associated with poorer functioning and more internalizing symptoms than no history of parental depression [6]. Overall, findings from these studies underscore the risk conferred by parental depression and suggest that these difficulties do not necessarily subside with parental recovery from depression. Earlier age of onset of depressive disorder in adult probands may be particularly associated with familiarity of depression [14,15].

## Bottom up studies of family aggregation

Given the association between age of onset of depressive disorders in depressed adult probands and familiarity of depression, a number of studies have used a “bottom-up” approach – selecting child/adolescent probands and examining parental psychopathology and family

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aggregation of mood disorders. To date, there have been eleven such studies with samples ascertained based on the presence of depressive disorders in youth that have met modern methodological standards; samples, methodology and findings from these studies are described in Table 1. These studies used structured assessments, operational

criteria for establishing diagnoses in childhood and adolescence, and evaluation of disorder in relatives by interviewers who were blind to proband diagnosis. Five of these studies included families of probands diagnosed with depression during childhood (ages 6-12) [16-20]; three studies evaluated families of probands identified with depression as

Authors	Journal	Sample referral source/ages	n/Diagnostic Group(s)	Assessment proband/ Relative	Findings
Harrington, Fudge, Rutter, Bredenkamp, Groothues & Pridham, 1993	British Journal of Psychiatry	Inpatient/ Children and adolescents (ages 6-16)	62 depressive syndrome 60 PC	Clinical data records/ SADS-L	Higher rates of depression in 1 <sup>st</sup> degree relatives of depressed probands. No differences by proband gender; however, female more likely than male relatives to be depressed. No differences in non-depression diagnoses, psychiatric admissions, or psychotropic medication use.
Klein, Lewinsohn, Seeley & Rohde, 2001	Archives of General Psychiatry	Community/ Adolescent 14-18 years old	268 MDD 110 PC (anxiety, substance use, disruptive behavior) 291 NC	KSADS/ SCID Family Informant Schedule	Higher rates of MDD in relatives of MDD probands compared to other two proband groups; not different by sex; among female MDD probands rate of MDD higher in female relatives.
Kovacs, Devlin, Pollack, Richards, Mukerji, 1997	Archives of General Psychiatry	Outpatient/ Children 8-13 years	99 depressive 26 BP 55 PC (primarily disruptive behavior)	Interview Schedule for Children/ SADS-L FHRDC	Youth with mood disorders (depressive or bipolar) had high odds of family alcoholism/substance use disorders and MDD, particularly in female relatives. BP probands had more lifetime mania in their families compared to other two groups.
Kutcher & Marton, 1991	J American Academy of Child & Adolescent Psychiatry	Inpatient & outpatient Adolescent (ages 13-19)	23 BP 26 MDD 24 NC	KSADS/ Family History method/	BP probands had higher rates of BP in 1 <sup>st</sup> degree relatives than NC and MDD probands. BP and MDD probands had higher rates of unipolar depression and other psychiatric disorders in 1 <sup>st</sup> degree relatives than NC probands.
Livingston, Nugent, Rader & Smith, 1985	American Journal of Psychiatry	Inpatient Children (ages 6-12)	12 Anxiety 11 Depression	DICA/ FHRDC/	Two groups very similar; only greater alcoholism in non-parent relatives of depressed probands
Mitchell, McCauley, Burke & Calderon, 1989	J American Academy of Child & Adolescent Psychiatry	Children – 31% inpatient 69% outpatient Adolescent – 100% outpatient	94 MDD (43 children; 51 adolescents) 38 PC (mixed)	KSADS for probands SADS-L for parents	No differences in rates of maternal or paternal depressive disorders; MDD probands had more maternal suicide attempts, anxiety and substance use disorders and more likely to have two depressed parents. Proband and parent suicidality not associated. Child more likely than adolescent MDD probands to have maternal substance use and suicidality.
Puig-Antich, Goetz, Davies & Kaplan, 1989	Archives of General Psychiatry	Outpatient/ Depression Clinic Referral Prepubertal Children (ages 6-12)	48 MDD 20 PC (primarily anxiety) 27 NC	K-SADS/ SADS FHRDC	More MDD in relatives of MDD probands than NC probands with PC probands in between and not different from other groups; more alcoholism in MDD compared to other groups. Comorbid MDD/ CD in probands associated with less MDD in relatives; proband psychotic depression associated with more MDD and bipolar disorders in relatives.
Todd, Neuman, Geller, Fox & Hickok, 1993	J American Academy of Child & Adolescent Psychiatry	Participating in antidepressant med trial/ Children (ages 6-12)	22 BP I or II 54 MDD 31 NC (parental mood disorder excluded)	KSADS/ FHRDC	High rates of BP I and unipolar depression in 1 <sup>st</sup> , 2 <sup>nd</sup> and 3 <sup>rd</sup> relatives of BP and MDD probands. MDD relatives of BP and MDD probands had earlier onset of MDD and greater likelihood of suicide attempts (but not completed suicide).
Weller, Kapadia, Weller & Fristad, 1994	Journal of Affective Disorders	Inpatients/ Children (ages 6-12)	63 MDD 63 PC (age/ gender matched; all disruptive behavior)	DICA/ Chart review	MDD probands had more familial MDD, any mood, ASP, anxiety and somatization disorders than did PC probands. MDD probands' mothers had more mood/anxiety disorders and fathers more antisocial personality. MDD probands with comorbid behavior disorders had more alcohol abuse and ASP in relatives than did those with comorbid anxiety.
Wickramaratne, Greenwald & Weissman, 2000	J American Academy of Child & Adolescent Psychiatry	Outpatient/ Children (prepubertal) Adolescent (postpubertal)	76 Prepubertal MDD 73 Postpubertal MDD 53 Prepubertal NC 25 Postpubertal NC	KSADS/ SADS FHRDC	Both prepubertal and postpubertal MDD probands, had more familial MDD than prepubertal and postpubertal NC. Only among prepubertal MDD was recurrence and continuity into adulthood (trend) associated with greater familial loading.
Williamson, Ryan, Birmaher, Dahl, Kaufman, Rao & Puig-Antich, 1995	J American Academy of Child & Adolescent Psychiatry	Outpatient Mood Specialty Clinic/ Adolescent (ages 12-17)	76 MDD 34 NC	KSADS/ SADS FHRDC	More MDD and any psychiatric disorder in 1 <sup>st</sup> degree relatives of MDD probands, but not more mania, schizophrenia, alcoholism, ASP, or drug use disorders. Suicidality aggregated in families of probands with MDD/Suicidality.

Note: KSADS – Schedule for Affective Disorders and Schizophrenia for School-Aged Children; SADS -- Schedule for Affective Disorders and Schizophrenia; DICA – Diagnostic Interview Schedule for Children; SCID – Structured Clinical Interview for the DSM; FHRDC – Research Diagnostic Criteria; MDD – Major Depressive Disorder; BP – Bipolar Disorders; PC – Psychiatric Controls; NC – nonpsychiatric controls; ASP – Antisocial Personality Disorder; CD – Conduct Disorders

**Table 1:** Bottom-Up Studies of Familial Aggregation of Depression.

adolescents [21-23]; and three studies assessed psychopathology in parents of both depressed children and adolescents [7,8,24]. Consistent with findings focusing on adults with depression, results indicate overall that youth with depression have significantly higher rates of depression in their parents as compared to control youth with no mental illness.

Findings are less clear when comparisons are made between relatives of youth with depressive disorders and relatives of youth with other psychiatric disorders. Some studies report elevated rates of depression in relatives of youth with depressive disorders in comparison to youth with non-mood psychiatric disorders [15,18,19,22], but others find no between group differences [14,16,23]. In most of these studies, psychiatric control groups were diagnostically heterogeneous. Interestingly, however, studies comparing youth with depressive disorders to psychiatric control groups composed primarily of probands with disruptive behavior disorders [17,20] were more likely to find significant between group differences in family aggregation of depressive disorders than were studies comparing depressed youth to control groups composed primarily of probands with anxiety disorders [16,18]. This could be due to common underlying etiologic factors across youth internalizing syndromes. Research with clearly defined comparison groups of youth with non-depressive psychiatric disorders is needed to resolve the issue of whether elevations in rates of depression in parents of depressed youth is related specifically to youth depression, or is common to a broad range of youth disorders or psychopathology in general.

Evidence of clinical and biological heterogeneity among youth and adults suffering from depression has led to increased focus on the identification of etiologically homogeneous subgroups [19,25,26]. Demonstration that a potential subgroup “breeds true” within families provides some support of the potential validity of that etiologic category [27]. Three studies [17,19,22] have included comparisons among youth with Major Depression (MDD), Bipolar (BP) disorders and nonpsychiatric controls. In all three, probands with mood disorders (either MDD or BP) had higher rates of MDD in relatives than did nonpsychiatric control probands; results were more mixed regarding differences between probands with mood disorders. Two studies suggested more lifetime mania/BP among relatives of BP probands [17,22], and another suggested no differences in BP I disorder among relatives from the two proband groups [19]. These findings are complicated by the fact that bipolar disorders may show initial presentation of depression, and therefore some youth with MDD will be misclassified, ultimately proving over time to be in the bipolar-spectrum.

Focusing on unipolar depression, past diagnostic systems have distinguished between MDD, dysthymic disorder (DD), and double depression defined as DD with superimposed periods of MDD (DD/MDD). These syndromes differ in both the severity of depressive symptoms and their chronicity/persistence: MDD is defined by severe symptoms with a brief duration criterion (at least 2 weeks); DD by less severe but more persistent symptoms, a minimum duration of 1 year; and DD/MDD as a more severe and chronic/persistent syndrome. Although DD is less severe in symptom profile than MDD, in adults its chronicity and associated psychosocial impairment may be equally, or more, burdensome [28]. In a naturalistic study of youth, DD was found to be particularly chronic with an average length of 3.9 years [29]. The potential for DD to disrupt psychosocial developmental is particularly underscored by findings that social functioning difficulties associated with depression often persist even after recovery from an index depressive episode [30]. DD/MDD appears

to represent a particularly severe and impaired subpopulation of depressed individuals [31]. The DSM-5 has now included a diagnosis of persistent depressive disorder which captures both DD and DD/MDD presentations. Chronic depression in adults may be associated with greater familial loading than nonchronic depression [32]; further, chronicity of depression in adult probands appears to be associated with chronicity of depression in relatives [25]. Early-onset DD (before age 21) appears to be more highly associated with family history of mood disorders than does late-onset DD (at 21 years of age or later) [33]. However, to our knowledge, there are no other published data on rates of dysthymic disorder or other forms of chronic depression in parents of youth with depressive disorders, nor have studies evaluated differences in rates of depressive disorders among youth with these different forms of depression.

### Current study

We address these issues using data from a controlled, blind, family study and examine rates of depressive disorders among fathers and mothers of probands with child and adolescent-onset depression (MDD, DD, and DD/MDD) and two comparison groups: 1) a psychiatric comparison group composed of never depressed youth with ADHD, and 2) community controls, with no histories of ADHD or depression. Past studies of family aggregation have compared youth with depression to youth with heterogenous disruptive behavior disorders. ADHD youth provide a particularly useful clinical comparison group given that ADHD, like depressive disorders in youth, are relatively common, associated with increased family stress, and are well-characterized and reliably assessed [34]. We hypothesized that there would be a higher rate of MDD, DD, DD/MDD and bipolar disorders in the parents of probands with child and adolescent-onset depression as compared to never depressed youth with ADHD and youth with no history of depression or ADHD. Additionally, we explored differences in parental mood disorders among the depressive subgroups (MDD, DD, DD/MDD) and hypothesized that probands with more chronic and severe youth depression (DD/MDD) would have higher rates of parental depression than would probands with less chronic (MDD) and less severe (DD) forms of depression.

## Method

### Participants

**Proband ascertainment:** The UCLA Program Project “Family studies of childhood psychiatric disorders” focuses on family studies of depression, attention deficit hyperactivity disorder (ADHD), and schizophrenia. This report focuses on relatives of three groups of probands: 1) probands with youth-onset depression (MDD and/or DD), with or without comorbid ADHD; 2) probands with ADHD but no history of depressive disorders; and 3) community controls with no histories of depression or ADHD. Criteria for inclusion in this study were: youth had to be between 6 and 18 years of age at time of diagnosis; have at least one biological parent who was willing to participate in the study; have a Full Scale IQ score  $\geq 70$ ; and meet DSM-III-R [35] diagnostic criteria for one of the three proband groups. Additional exclusionary criteria were evidence of significant neurological or medical disorder, or adopted.

We ascertained probands through a variety of sources including inpatient and outpatient mental health centers, schools, community outreach, and advertisements. Lists of potential participants living in the same ZIP codes as youth recruited through other sources were obtained from a scientific survey research firm (Survey Sampling Inc,

Fairfield, Conn). Parents of potential participants were contacted by telephone to explain the purpose of the study and determine whether the youth met study inclusion and exclusion criteria. All participants in the study provided informed consent or assent (for participants <18 years of age). Probands were enrolled between Sept 1992 and May 1998. Information on referral sources is listed in Table 2.

**Proband diagnosis:** Final best estimate diagnoses for all probands were based on child and parent interviews using the Program Project version of the Schedule for Affective Disorders and Schizophrenia for School Age Children (K-SADS) [36], which supplemented the K-SADS-Epidemiologic version (K-SADS-E) [37] with sections from the K-SADS-Present Episode [38] on current severity of depression and anxiety. Because the study began before DSM-IV criteria [39] were finalized, DSM-III-R [35] diagnostic criteria were used in order to maintain consistency throughout the study. The diagnostician who conducted the interviews reviewed the diagnostic interviews and ancillary information (case records) with a senior clinician (DPC or JRA) to reach a final consensus diagnosis. Interviewers received extensive training prior to conducting project interviews. For all staff interviews, training involved review of the diagnostic protocol,

review and rating of 5 training tapes, and review and rating of 5 of the interviewer's tapes by a senior diagnostician. Estimates of inter-rater agreement based on 49 cases independently rated by 2 diagnosticians indicated good reliability for the major diagnoses used in this study, kappas ranged from 0.77 to 0.86.

### Diagnosis of first-degree relatives

All diagnostic data on relatives was collected and reviewed by diagnosticians who were blind to proband diagnosis. Parents were interviewed with the SADS-L [40]; and, when possible, both parents were directly interviewed. Additionally, both in cases with and without direct interviews with both parents, family history of a major psychiatric illness in the other parent was elicited using the Family History Interview of Psychiatric Status [41]. Final best estimate diagnoses were based on a review of all diagnostic information for the relative by the interviewer and a senior clinician (DPC or JRA) who was blind to proband diagnosis. Interviewer training was as described above for K-SADS. Estimates of inter-rater agreement between two independent raters, based on 76 cases, were adequate for diagnoses, kappas ranged from 0.73 to 0.82.

	Depressed (N = 127)	ADHD (N = 116)	Community Control (N = 78)
<b>Proband Age</b>			
Mean (SD)	12.29 (2.81) <sup>a</sup>	9.81 (2.76) <sup>b</sup>	11.67 (3.03) <sup>ac</sup>
Range	6.00 - 18.00	6.08 - 16.00	6.33 - 17.42
<b>Proband Gender</b>			
m:f	84 : 43	85 : 31	51 : 27
% male	66%	73%	65%
<b>Proband Ethnicity</b>			
Caucasian	97 (76.4%)	89 (76.7%)	54 (69.2%)
Latino/Hispanic	9 (7.1%)	10 (8.6%)	9 (11.5%)
African-American	7 (5.5%)	8 (6.9%)	7 (9.0%)
Asian	3 (2.4%)	1 (0.9%)	2 (2.6%)
Other	11 (8.7%)	8 (6.9%)	6 (7.7%)
<b># Mothers</b>	127	116	78
<b># Mothers with direct interviews</b>	121 (95%)	115 (99%)	75 (96%)
<b># Fathers</b>	123	115	76
<b>#Fathers with direct interviews</b>	82 (67%)	96 (83%)	39 (51%)
<b>Mother's Age</b>			
Mean (SD)(N)	41.76(6.04) <sup>b</sup>	40.28(5.69) <sup>a</sup>	42.69(5.38) <sup>b</sup>
Range	27.14 - 55.97	25.64 - 53.47	25.00 - 54.42
<b>Father's Age</b>	44.85 (7.54) 29.0-64.78	43.63 (6.45) 26-63.88	44.87 (6.39) 25.47-57.00
<b>Family Composition</b> n(%) Lives With Both Parents	70 (55.1%)	76 (65.5%)	61 (78.2%)
<b>Recruitment Source</b>			
Inpatient	11 (8.7%)	0	0
Outpatient	48 (37.8%)	43 (37.1%)	10 (12.8%)
Schools	29 (22.8%)	26 (22.4%)	8 (10.3%)
Survey Sampling	2 (1.6%)	0	34 (43.6%)
Other	37 (29.1%)	47 (40.5%)	26 (33.3%)
<b>Proband Diagnoses</b>			
Major Depression(MDD)	90 (76.4%)	0	0
Dysthymic disorder(DD)	66 (52.0%)	0	0
DD/MDD	36 (28.3%)	0	0
ADHD	46 (36.2%)	102 (87.9%)	0
ADD, no ADHD	1 (8%)	14 (12.1%)	0
Anxiety Disorder	54 (42.5%)	22 (19%)	6 (7.7%)
Conduct Disorder	17 (13.4%)	10 (8.6%)	0
Oppositional Disorder	61 (48%)	45 (38.8%)	4 (5.1%)

Notes: Due to n<5 for some cells, cells were collapsed as follows for analyses examining between group differences: ethnicity analyses compared Caucasian, Latino/Hispanic, African-American, Other. Recruitment source analyses compared clinical vs. other. Groups with the same superscripts (i.e. <sup>a,a</sup>) did not differ; those with different superscripts (i.e., <sup>a,b</sup>) were significantly different (p<0.05). All youth who met criteria for diagnoses of MDD or DD are included in the rows for these diagnoses. There were 36 youth who met criteria for both MDD and DD (Double Depression), 61 youth who met criteria for MDD but not DD, and 30 youth who met criteria for DD but not MDD.

Table 2: Description of the sample.

## Statistical methods

Given that not all parents had passed through the age of risk for the development of mood disorders, survival modeling was used to estimate lifetime morbid risk. Survival functions were calculated based on an extension of the Kaplan-Meier life table method as operationalized in the LIFETEST procedure in SAS. These calculations estimate risk across different parent ages. Due to between group differences in proband age, we tested for between group differences in survival curves using proportional hazard regression models adjusting for proband age. Analysis of variance and t-tests were used to assess between group differences on continuous variables;  $\chi^2$  analyses or Fisher exact test (if the minimum expected cell size was  $\leq 5$ ) were used for dichotomous variables. Where parents were unable to give an exact age of onset, we clarified whether onset was during childhood, adolescence, adulthood, or unknown. For these cases, we used multiple imputation with 10 imputations and calculated a mean age of onset which was used to generate the survival curves.

## Results

### Characteristics of probands and relatives

Table 2 presents descriptive information on participants in each group. Probands ranged in age from 6 to 18 years. The never depressed ADHD probands were significantly younger than the depressed,  $t(242) = 6.81, p < 0.01$ , and community control probands,  $t(205) = 4.46, p < 0.01$ . This may have been due to the fact that the risk of depression increases with age, and youth with histories of both ADHD and depression were placed in the depressed group in order to ensure a never depressed ADHD comparison group. The sample was predominantly male (65-73% across groups) and Caucasian (69-76% across groups). Most children lived with both of their parents, although this varied across groups,  $\chi^2(1) = 11.33, p < 0.004$ . Depressed probands were least likely

to live with both parents and the community controls were most likely to live with both parents. As expected, given the group differences in proband age, there was also a significant difference between groups in mother's age,  $F(2,318) = 4.36, p < 0.014$ , with younger age among mothers of youth in the ADHD group. Similar patterns were observed for fathers, but these differences did not reach statistical significance.

As illustrated in Table 3, most mothers completed the direct SADS interviews (311/321, 97%) and data were available on all mothers when direct plus indirect interviews were used. Participation was lower for fathers: 217 fathers completed direct SADS interviews (217/321, 68%), but combined SADS or FIPS data was available for 314 fathers (314/321, 98%).

Risks of depressive disorders are presented separately for mothers and fathers. Analyses were conducted both based on direct interviews and based on combined direct and indirect diagnostic interviews. Given the high percentage of direct interviews for mothers, we have included only these data for mothers in Table 3 and only report these findings in text. Alternatively, given that approximately 1/3 of fathers did not provide direct interviews, we have included findings based on both direct and indirect interviews in Table 4 and discuss the differences in findings between these two approaches in text. Results were generally similar for these different analyses, suggesting that our findings are relatively robust to sampling variations.

### Risk for depressive disorders in mothers

As illustrated in Table 3, which presents the results of the life table analyses, mothers of depressed probands had the highest prevalence of depressive disorders. Based on results of direct interviews only, the risk of major depression was significantly higher among mothers of depressed probands when compared to mothers of control probands and when compared to mothers of ADHD probands; however, rates

	Proband Diagnosis			Wald $\chi^2$		
	Dep n = 127	ADHD n = 116	CC n = 78	Dep vs. CC	Dep vs. ADHD	ADHD vs. CC
Major Depression	0.63	0.50	0.36	12.19****	5.67*	1.83
Recurrent Depression	0.41	0.26	0.17	9.028***	9.05***	0.116
Dysthymic Disorder	0.24	0.18	0.07	7.74**	3.20*	1.94
Double Depression	0.21	0.11	0.05	6.91*	4.49*	1.00

Note: Direct Interview Data Only. Morbid Risk is determined at age 45 to ensure comparable estimates across groups. Dep = Depression; ADHD = Attention Deficit Hyperactivity Disorder; CC = community controls.

\* $p < 0.10$ , \*\* $0.05$ , \*\*\* $0.01$ , \*\*\*\* $0.001$

Table 3: Risk for Depressive Disorders as Determined by Life Table Analyses. Mothers of 3 groups of Child Probands

		Proband Diagnosis			Dep vs. CC	Dep vs. ADHD	Dep vs. CC
		Dep (n = 82) (n = 123)	ADHD (n = 96) (n = 115)	CC (n = 39) (n = 76)			
Major Depression	Direct	0.33	0.28	0.26	1.77	3.49*	0.01
	D + I	0.30	0.24	0.19	4.48*	5.01*	0.03
Recurrent Depression	Direct	0.17	0.11	0.15	0.97	4.71*	0.66
	D + I	0.13	0.09	0.08	1.72	3.57	0.16
Dysthymic Disorder	Direct	0.18	0.08	0.05	3.89*	5.37*	0.31
	D + I	0.15	0.08	0.02	6.74**	4.78*	1.58
Double Depression	Direct	0.12	0.04	0.03	2.72*	4.28*	0.18
	D + I	0.08	0.03	0.01	4.08*	4.21*	0.56

Notes: Direct = Direct Interview Data Only; D + I = Direct and Indirect Interview Data. Morbid Risk is determined at age 45 to ensure comparable estimates across groups. Dep = Depression; ADHD = Attention Deficit Hyperactivity Disorder; CC = community controls.

\* $p < 0.10$ , \*\* $0.05$ , \*\*\* $0.01$

Table 4: Morbid Risk for Depressive Disorders as Determined by Life Table Analysis in Fathers of 3 Groups of Child Probands.

of major depression in mothers of ADHD probands did not differ significantly from those for mothers of control probands. When the more restrictive diagnosis of recurrent major depression was employed, similar results were obtained. The risk of recurrent major depression was significantly higher for mothers of depressed probands as compared to mothers of community controls or mothers of ADHD probands, and no significant differences were found between the ADHD and control groups. The risk of maternal dysthymic disorder was lower than that for maternal major depression. However, the risk of dysthymic disorder was significantly higher for mothers of depressed probands as compared to mothers of community controls and marginally higher as compared to mothers of ADHD probands with no significant differences between mothers of probands in the ADHD and control groups. Rates of double depression, major depressive disorder superimposed on dysthymic disorder, were significantly higher among mothers of depressed probands as compared to mothers of community controls and mothers of ADHD probands. Results based on direct and indirect interviews were nearly identical.

### Risk for depressive disorders in fathers

Rates of depressive disorders were lower among fathers than mothers. As shown in Table 4, which presents results of the life table analyses for fathers, across all types, depressive disorders were more common among fathers of depressed probands vs. the other groups. However, results were weaker than those for mothers. The strongest and most consistent results emerged for rates of dysthymic disorder where the risk of dysthymic disorder was significantly higher among fathers of depressed probands when compared to fathers of either community controls ADHD probands using combined direct and indirect interviews. Similarly, the risk of double depression was significantly higher among fathers of depressed probands when compared to fathers of ADHD probands using combined interviews. The findings for double depression were attenuated to the trend level when the analyses used direct interview data only. A significantly higher risk of double depression was also found for fathers of depressed probands vs. community controls using the combined direct and indirect interview data, but these groups were only marginally different in analyses of direct interview only. The risk of major depression in fathers of depressed probands was significantly higher than that for fathers of ADHD probands,  $\chi^2(1) = 5.01, p < 0.05$ , and for fathers of community controls using combined direct and indirect interview data; only a marginal difference was retained between the fathers of depressed probands and community control probands when only interview data were used. The risk of recurrent depression was significantly higher among fathers of depressed probands vs. ADHD probands using direct interview data only. There were no differences on any depression diagnoses for fathers of probands in the community control and ADHD groups.

### Risk for parental bipolar disorders

The rate of bipolar disorder was relatively low in this sample and due to the low frequency we present only descriptive data. Eight mothers had bipolar I disorder by direct interview, with no additional cases identified through indirect interviews. Six of these 8 mothers were from the depressed group (75%) The other two cases were split between the ADHD and CC groups. There were 12 mothers with Bipolar II disorder and the distribution was similar across groups (depressed=4, ADHD= 5, CC=3). All mothers with Bipolar II disorder were identified through direct interviews with no additional cases identified through the indirect interviews.

In fathers, by direct interview there were 3 fathers with Bipolar I Disorder (2 in the depressed group and 1 in ADHD group) and 6 fathers with Bipolar II Disorder (3 in the depressed group and 3 in ADHD group). When indirect interview data were examined, 3 additional cases of Bipolar I disorder were identified, resulting in 6 cases with Bipolar I (5 in the depressed group, 1 in the ADHD group). There were no additional cases of Bipolar II Disorder in fathers using indirect interviews.

### Heterogeneity among youth with depressive disorders

In Table 5 rates of maternal Major Depressive Disorder, Recurrent Depression, Double Depression and Dysthymic Disorder are compared for probands with MDD alone, DD alone and MDD/DD. Consistent with the view of double depression as the most severe form of depressive disorder in youth, there was a significantly higher risk of major depression among mothers of youth with double depression when compared to mothers of youth with major depressive disorder and no DD, and a marginally higher risk of major depression when compared to mothers of youth with DD and no MDD. As illustrated in Table 5, maternal rates of both recurrent MDD and Double Depression were higher in MDD/DD probands than in those with MDD or DD alone.

### Discussion

We examined rates of parental mood disorders in three child/adolescent proband groups – a group suffering from depressive disorders (with or without comorbid ADHD), a group with ADHD and no history of depression, and a community control group selected for the absence of lifetime diagnoses of depression and/or ADHD. The present results underscore the familiarity of youth depression and suggest that increased rates of parental depression may be specifically associated with youth depression rather than a function of youth psychopathology more generally. In addition, the present findings suggest that severity/chronicity of youth depression may be an indicator of increased risk for parental depression.

This study clearly documents an elevated rate of depressive disorders

	Proband Diagnosis			Wald $\chi^2$		
	MDD/DD n = 36	MDD N = 61	DD n = 30	MDD/DD vs. MDD	MDD/DD vs. DD	MDD vs. DD
Major Depression	0.77	0.51	0.63	7.71**	5.67*	1.83
Recurrent Depression	0.41	0.26	0.17	9.03***	9.05***	.116
Dysthymic Disorder	0.24	0.18	0.07	7.74**	3.20*	1.94
Double Depression	0.21	0.11	0.05	6.91**	4.49*	1.00

Notes: Direct Interview Data Only. Morbid Risk is determined at age 45 to ensure comparable estimates across groups. MDD = Major Depressive Disorder; DD = Dysthymic Disorder; MDD/DD = Double Depression (MDD + DD).

\*p < 0.10, \*\*0.05, \*\*\*0.01, \*\*\*\*0.005, \*\*\*\*\*0.001

**Table 5:** Risk for Depressive Disorders as a Function of Proband Depression Subtype as Determined by Life Table Analyses. Mothers of 3 groups of Child Probands.

in both mothers and fathers of children suffering from depressive disorders, relative to both never depressed children with ADHD and community controls. Across a spectrum of depressive diagnoses in the probands, mothers of depressed youth consistently had elevated rates of major depressive disorder, recurrent major depression, and double depression (major depression superimposed on dysthymic disorder). Although dysthymic disorder was a less frequent diagnosis, mothers of depressed youth also showed elevated rates relative to community controls and a trend for higher rates than ADHD controls.

Fathers of depressed youth had lower rates of depression than did mothers of depressed youth, consistent with epidemiologic data indicating gender differences in prevalence of depressive disorders [42,43] with women having almost twice the lifetime risk as compared to men. While results were weaker for fathers than for mothers, our data still point to an increased likelihood of depressive disorders in fathers of depressed youths compared to youth with ADHD and to community controls, including higher rates of dysthymic disorder as well as double depression and recurrent depression. Thus, fathers as well as mothers of depressed youths are likely to suffer from depression, and these data underscore the importance of considering fathers.

Overall, our findings are consistent with other studies that included normal control groups [18,19,21-24] in suggesting elevated rates of parental depression among depressed youth. Further, the present findings were consistent with studies using psychiatric control groups consisting of youth with disruptive behavior disorders [8,17,20] in suggesting that parental depression, while not unique to youth with depression, is certainly elevated. Our data cannot speak to differences in family aggregation between youth with depression and those with other internalizing disorders, such as anxiety, which may share common underlying etiologic factors [44,45].

Our findings are in line with other studies suggesting that chronicity may be an important specifier in depressive disorders. Recent meta-analyses of genome-wide association studies of mood disorders underscore the complexity of multigenic mechanisms likely underlying vulnerability to depressive disorders and emphasize the need to examine homogenous groups – with recurrent, persistent and early onset depression a major focus [46,47]. In the present study, when compared to either major depression or to dysthymic disorder alone, major depression imposed on dysthymic disorder, or “double depression”, in youth was clearly associated with higher rates of maternal depressive disorders. Indeed, these results combined with findings with adults with depression [31-33], suggest that chronic depression may be associated with greater familiarity in both adults and youth than other forms of depression. It is important to note that in this study dysthymic disorder, which is characterized by chronicity, was not associated with greater maternal depression compared to major depressive disorder in youth. Indeed, the highest rates of maternal depression were only associated with double depression, which is characterized by both chronicity and severity. The DSM-5 category of persistent depressive disorder [34] was designed to capture both dysthymic disorder and double depression; our data would suggest these two variants may have important distinctions and possibly different underlying pathways.

Given the low rates of bipolar disorders in parents across all groups of youth in our study, it was not possible to conduct statistical tests and to draw conclusions about the relative risk of parental bipolar disorder as a function of youth psychopathology from this study. Bipolar I disorder occurred with disproportionate frequency among parents of youth with depression as compared to parents of youth with ADHD or parents of community control youth. The case was less clear for Bipolar II, where

cases appeared to be more equally distributed between the ADHD and depressed proband groups. Among adults, bipolar disorders tend to aggregate in families of individuals with bipolar disorder compared to individuals with unipolar depression [2], and our sample only included youth with unipolar depression. However, there is some question as to whether Bipolar II disorder falls on the unipolar mood disorder spectrum [48]. Some studies suggest that narrow spectrum bipolar disorder in youth is associated with both parental Bipolar I and Bipolar II disorders [49], and one recent study of family aggregation indicated that, while frequently comorbid, depression and mania may represent unique underlying pathways [5]. Future studies are needed to fully clarify the aggregation of depression and bipolar disorders in families of depressed versus bipolar youth.

The current study has a number of limitations. First, probands in the ADHD and depression groups were recruited primarily through clinics, referrals from practitioners and school personnel. Samples recruited from such clinical sources may be subject to “Berkson’s bias,” meaning that compared to youth recruited from community sources, they are likely to be more impaired, of European heritage, to have higher comorbidity and to be less likely to be girls [50]. This selection bias may limit our ability to generalize findings to larger community samples. It is possible that depression and ADHD in our samples include more severe forms with higher family loading than would be evident in community samples, although our data point to elevated rates of depression in parents of depressed probands relative to ADHD probands even within such a clinical sample.

Second, although this study represents the largest sample to date to include direct interviews with fathers, 1/3 of fathers did not provide direct interviews. Findings were generally consistent whether cases with only direct (maternal report) interviews or direct (father report) and indirect interviews were considered in the analyses, thus increasing confidence in these findings. Third, although findings from this study clearly suggest elevated levels of parental depression among youth with depressive disorders, they cannot tell us the underlying reasons for these differences. In their seminal paper on the association between maternal and child depression, Goodman and Gotlib [51] outline a number of possible mechanisms, including biological (heritability; innate dysfunctional neuroregulatory mechanisms) and psychosocial (exposure to negative maternal cognitions, behavior and affect; stress context) transmission. In the present study, it is also possible that child depressive disorder impacted the development of depressive disorders in parents. The study began prior to DSM-IV and 5. Diagnoses were derived using DSM-III-R criteria, and results might have differed somewhat with current criteria, although changes have been relatively minimal for depressive disorders across these different DSM versions [34,35,39,52,53].

In clinical practice, these results underscore the critical need to both evaluate parents of depressed youths for depression and engage in selected prevention strategies for both parents and youth at risk for depression [9]. Given data indicating a poor response to treatment among youths whose parents suffer from depression [54], it may be that addressing the treatment needs of parents is a critical component of effective treatment for depression in children [55]. A number of strategies have been developed for addressing both the mental health needs of parents and to prevent cycles whereby parent and youth depression interact to increase stress and dysfunction across family members [56,57]. Future research is needed to clarify optimal approaches for addressing the needs of parents when treating youths suffering from depression.

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