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Psychopathology in the adolescent and young adult offspring of a community sample of mothers and fathers with major depression

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ABSTRACT

Background. There is a large literature indicating that the offspring of mothers with Major Depressive Disorder (MDD) are at increased risk for depression. However, much less is known about the effects of paternal MDD on offspring psychopathology.

Method. We addressed this issue using a large community sample of parents and their adolescent and young adult offspring ($n=775$). Parents and offspring were independently assessed with semi-structured diagnostic interviews. Offspring were interviewed three times from mid-adolescence to age 24 years.

Results. Maternal MDD was significantly associated with offspring MDD. Paternal MDD was also significantly associated with MDD in offspring, but only among offspring with depressive episodes of moderate or greater severity. These effects persisted after controlling for socio-economic status, family intactness, and non-mood disorders in both parents. Rates of MDD were particularly elevated in offspring of mothers and fathers with early-onset MDD, and offspring of fathers with recurrent MDD. The magnitude of the associations between MDD in parents and offspring was generally in the small-to-medium range.

Conclusions. These results confirm previous findings of elevated risk of MDD in the offspring of depressed mothers. In addition, the results suggest that MDD in fathers is associated with increased risk of depression in offspring, but that it is limited to MDD episodes in offspring of moderate or greater severity.

INTRODUCTION

Numerous studies have reported that the school-aged, adolescent, and young adult offspring of mothers with Major Depressive Disorder (MDD) exhibit elevated rates of MDD, as well as a variety of non-mood disorders (Weissman *et al.* 1997; Beardslee *et al.* 1998; Goodman & Gotlib, 1999). However, few data are available on the risk of MDD and other forms of psychopathology in the offspring of depressed fathers. This is probably due to the higher prevalence of depression in women, the greater difficulty in recruiting fathers for research, and the assumption that mothers generally have a larger impact on children due to their greater role in child-rearing (Phares, 2002).

The few studies that have examined the risk for MDD in offspring of depressed fathers have produced inconsistent results. Thus, some studies have reported elevated rates of MDD in offspring of depressed fathers compared to offspring of controls (e.g. Orvaschel *et al.* 1988; Nomura *et al.* 2001), but other studies have failed to find differences (e.g. Keller *et al.* 1986).

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Most of this literature has relied on clinical samples, which are not representative of depression in the community (Costello, 1993). Moreover, because women are more likely to seek treatment for depression than men (Moeller-Leimkuehler, 2002), there may be even greater bias in clinical samples of depressed fathers than clinical samples of depressed mothers.

We are aware of only two studies that have examined rates of MDD in both depressed mothers and depressed fathers using large community samples. Lieb *et al*. (2002) reported that both maternal MDD and paternal MDD were associated with increased rates of MDD in adolescent and young adult offspring. A limitation of this study, however, is that it relied entirely on offspring reports of parental psychopathology for the older (age 18–24 years) half of the sample, and conducted direct interviews with only one parent (generally the mother) for the younger (age 14–17 years) half of the sample. In contrast, Brennan *et al*. (2002) found that maternal depression (MDD or dysthymia), but not paternal depression was associated with depression in offspring. However, Brennan *et al*.'s (2002) sample was limited to families that were intact or where the offspring had substantial contact with the father, which may have excluded some of the fathers with the most significant psychopathology. Moreover, Brennan *et al*. (2002) included both biological fathers and stepfathers in their sample.

A number of studies have also suggested that particular characteristics of parental MDD, such as severity, chronicity, recurrence, and early age of onset, are associated with particularly elevated risks in offspring (Keller *et al*. 1986; Klein *et al*. 1988; Warner *et al*. 1995; Hammen & Brennan, 2003). However, most of these studies have been limited to depressed mothers or have combined depressed mothers and fathers. Hence, it is not clear whether these findings apply to paternal MDD or only to maternal MDD.

The present paper uses data from the Oregon Adolescent Depression Project (OADP; Lewinsohn *et al*. 1993) to examine the associations between maternal and paternal MDD and rates of psychopathology in their adolescent and young adult offspring in a large community sample. In addition, we explored the associations between the clinical features of maternal and paternal MDD and rates of MDD in offspring.

Table 1. *Flow chart depicting how sample was obtained*

T1 assessment
$n = 1709$ adolescents
T2 assessment
$n = 1507$ (88·2% of T1 sample)
T3 assessment
$n = 1101$ selected for assessment[a]
$n = 941$ completed T3 assessment (85·5% of those selected)
Parents
Of 1101 adolescents selected for T3 assessment, diagnostic data obtained on 837 biological mothers (76·0%) and 819 biological fathers (74·4%)
Exclusion criteria
62 families met exclusion criteria[b]
Final sample
775 offspring, 775 biological mothers, 758 biological fathers

[a] All adolescents with a lifetime history of psychopathology at T2 and non-whites were selected for inclusion in the T3 assessment, and a random sample of 457 white adolescents with no history of psychopathology was also targeted for inclusion.

[b] Families with one or more parents with a history of a non-affective psychotic disorder, bipolar disorder, or dysthymic disorder with no lifetime history of MDD were excluded. For one of the excluded families, information was available for only the biological mother.

In previous papers from the OADP we reported the results of a bottom-up family study of the first-degree relatives of the depressed and non-depressed adolescents (Klein *et al*. 2001, 2002). This article extends our previous papers by presenting a top-down high-risk study of depressed and non-depressed parents, examining psychopathology in the adolescent offspring, who have now been followed into early adulthood. Although top-down and bottom-up designs are closely related, they can yield different results, as the groups of offspring of depressed parents and youngsters with depression exhibit only partial overlap. This article also differs from our previous papers in that we focus exclusively on parents rather than using all first-degree relatives, take the temporal relationship between the onset of parent and offspring disorders into account, and include data on offspring through age 24 years.

METHOD

Participants

Offspring

An outline of the study design and number of participants at each stage is presented in Table 1. Offspring were randomly selected from nine

senior high schools in western Oregon. A total of 1709 adolescents (ages 14–18 years; mean age 16·6, S.D. = 1·2) completed the initial (T1) assessments between 1987 and 1989. The participation rate at T1 was 61%. Approximately 1 year later, 1507 of the adolescents (88%) returned for a second evaluation (T2). Several checks were conducted to assess the representativeness of the sample (see Lewinsohn *et al.* 1993 for details). Briefly, adolescents who did and did not participate in the T1 assessment were similar on intactness of the family and family size, but participants were more likely to be female, in a higher grade, and their parental socio-economic status was higher than non-participants. Of the adolescents who participated in the T1 assessment, those who also participated at T2 were more likely to be female, came from larger families, had a higher parental socio-economic status, and were less likely to have had a T1 diagnosis of a disruptive behavior disorder, and, for males only, a T1 substance use disorder, compared to those who did not participate at T2. However, among T1 participants, those who did and did not participate at T2 were similar on race, grade level, and all other T1 current and lifetime diagnoses.

At age 24 years, all adolescents with a history of MDD through T2 ($n = 360$) or a history of non-mood disorders through T2 ($n = 284$), and a random sample of adolescents with no lifetime history of psychopathology through T2 ($n = 457$) were invited to participate in a third (T3) evaluation. All non-white T2 participants were retained in the T3 sample to maximize ethnic diversity. Of the 1101 T2 participants selected for a T3 interview, 941 (85%) completed the age 24 evaluation. The T2 diagnostic groups did not differ on the rate of participation at T3.

Parents

We assessed lifetime psychopathology in the biological parents of the OADP participants in the T3 evaluation. To supplement the direct interviews and to ensure that at least some data were available for parents who could not be directly interviewed, informant data were obtained from the OADP participants, and, when parents were not available for direct interview, from a second informant (generally the co-parent or a sibling). Of the 1101 offspring selected for a T3 interview, diagnostic information on at least one biological parent was available for 837 (76%), including 837 mothers and 819 fathers. Of the 941 offspring with T3 data, parent diagnostic data were available for 801 (85%). In addition, there were 36 offspring with parent diagnostic information who did not complete a T3 evaluation. For these participants, offspring data were only available through T2.

Offspring diagnoses were based on DSM-III-R criteria (APA, 1987). Parent diagnoses were based on DSM-IV criteria (APA, 1994). All offspring with data on at least one parent were included in this report except for offspring of parents with a history of a non-affective psychotic disorder, bipolar disorder, or dysthymic disorder with no lifetime history of MDD ($n = 62$).

Only one child (the original OADP participant) per set of parents was included in the analyses. Although we also have diagnostic data on most siblings of the OADP participants, these data were collected at only one point in time using a different diagnostic interview, and the siblings had a wide range of ages. Hence, siblings were not included in the present report.

This article included data on 775 mothers, 758 fathers, and 775 offspring. Direct interviews were obtained from all of the offspring, 74·6% of the mothers and 46·4% of the fathers. Of the parents who were not directly interviewed, we obtained family history data from two or more informants for 40·6% of the mothers and 66·5% of the fathers.

Diagnostic assessments

Offspring

At T1, offspring were interviewed with a version of the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS; Orvaschel *et al.* 1982), which combined features of the Epidemiologic and Present Episode versions, and included additional items to derive DSM-III-R diagnoses. At T2 and T3, offspring were interviewed using the Longitudinal Interval Follow-up Evaluation (LIFE; Keller *et al.* 1987), which elicited detailed information about the onset and course of psychiatric disorders since the previous evaluation. In the present paper, offspring diagnoses are lifetime diagnoses derived from direct

interviews through the last available follow-up (which, in almost all cases, was T3).

To assess inter-rater reliability, independent raters reviewed audiotapes of a random sample of interviews (*n*'s ranged from 166 to 233). The reliability of lifetime diagnoses was fair to excellent for MDD [Kappa (κ) for T1, T2, and T3 was 0·86, 0·75, and 0·86 respectively], any anxiety disorder (κ for T1, T2, and T3 was 0·53, 0·66, and 0·84 respectively), and any substance use disorder (κ for T1, T2, and T3 was 0·89, 0·84, and 0·81 respectively).

Parents

Parents were interviewed using the *Structured Clinical Interview for DSM-IV Axis I Disorders, Non-Patient Version* (SCID-NP; First *et al.* 1996). All interviews were conducted without knowledge of the offspring's diagnoses. Independent raters reviewed audiotapes of 184 randomly selected interviews. The inter-rater reliability of lifetime diagnoses were excellent for MDD ($\kappa = 0{\cdot}94$), any anxiety disorder ($\kappa = 0{\cdot}90$), alcohol abuse/dependence ($\kappa = 0{\cdot}86$), and drug abuse/dependence ($\kappa = 0{\cdot}89$).

Family history data were collected using the *Family Informant Schedule and Criteria* (FISC; Mannuzza & Fyer, 1990), supplemented with all items necessary to derive DSM-IV diagnoses. Independent raters reviewed audiotapes of 242 randomly selected informant interviews. The inter-rater reliability of lifetime diagnoses were good to excellent for MDD ($\kappa = 0{\cdot}90$), any anxiety disorder ($\kappa = 0{\cdot}77$), alcohol abuse/dependence ($\kappa = 0{\cdot}90$), and drug abuse/dependence ($\kappa = 0{\cdot}82$).

We examined the sensitivity and specificity of informants' reports by comparing FISC diagnoses to SCID diagnoses for parents who had both sources of data available. Sensitivity varied according to the informant and target, but specificity was consistently acceptable. With the index offspring as the informant, sensitivity and specificity for MDD in mothers ($n = 523$) was 0·45 and 0·85 respectively; sensitivity and specificity for MDD in fathers ($n = 316$) was 0·32 and 0·90 respectively. With another family member as the informant, sensitivity and specificity for MDD in mothers ($n = 59$) was 0·30 and 0·80 respectively; sensitivity and specificity for MDD in fathers ($n = 40$) was 0·66 and 0·82 respectively. The greater sensitivity of offspring reports of maternal than paternal MDD probably reflects children's greater contact with, and knowledge of, their mothers than their fathers. The high sensitivity of other family members' reports of paternal MDD probably reflects the fact that the other family member informant was generally the mother, and mothers tend to have the best knowledge of family members (Cohen, 1988).

Consistent with previous research (Kendler *et al.* 1991; Chapman *et al.* 1994), sensitivity was somewhat higher and specificity was somewhat lower for informants who themselves had psychopathology. For example, the sensitivity and specificity of offspring reports of maternal MDD ($n = 258$) was 0·54 and 0·75 respectively, for offspring with a history of MDD themselves. For offspring with no lifetime history of MDD, the sensitivity and specificity of offspring reports of maternal MDD ($n = 265$) was 0·34 and 0·95 respectively. Similarly, the sensitivity and specificity of offspring reports of paternal MDD was 0·38 and 0·83 ($n = 144$) for offspring with a history of MDD, and 0·24 and 0·96 ($n = 172$) for offspring with no lifetime history of MDD. Finally, the correlations between informants' reports of the age of onset of MDD on the FISC and parents' reports of age of onset of MDD on the SCID for cases in which both the parent and informant agreed on the presence of MDD were 0·43 for mothers ($n = 77$, $p < 0{\cdot}001$) and 0·47 for fathers ($n = 26$, $p < 0{\cdot}05$).

As data were available from multiple informants for most parents, we derived lifetime DSM-IV diagnoses for the parents using the 'best-estimate' procedure (Leckman *et al.* 1982). Two diagnosticians, from a team of four senior clinicians, independently reviewed all information from the SCIDs and FISCs without knowledge of offspring diagnoses, and made best-estimate diagnoses for the parents using the guidelines in Klein *et al.* (1994). The diagnosticians' conclusions were then compared, and disagreements were resolved by consensus. Inter-rater reliability of the independently derived best-estimate diagnoses prior to the resolution of discrepancies was excellent for MDD ($\kappa = 0{\cdot}91$), any anxiety disorder ($\kappa = 0{\cdot}94$), alcohol abuse/dependence ($\kappa = 0{\cdot}97$), and drug abuse/dependence ($\kappa = 0{\cdot}96$).

Offspring interviews at T3 and interviews with relatives and informants were conducted by

telephone, which generally yields comparable results to face-to-face interviews (Sobin *et al.* 1993; Rohde *et al.* 1997). Most of the interviewers had advanced degrees in clinical or counseling psychology or social work, and several years of clinical experience. All interviewers were trained in the use of the diagnostic instruments and completed a minimum of two supervised training interviews, achieving $\kappa = 0{\cdot}80$ or better for concordance between their symptom ratings and those of the supervisor.

Other diagnostic issues

As discussed below, the lifetime prevalence of MDD through age 24 years in the OADP adolescents and young adults was higher than anticipated, probably due to the study's intensive surveillance (three comprehensive diagnostic evaluations between mid-adolescence and early adulthood). Thus, it is likely that many of the MDD episodes that we detected were relatively mild and transient (despite meeting full criteria for MDD). In light of this possibility, we chose to supplement DSM-III-R criteria for MDD with a second, higher threshold, definition of caseness that required at least a moderate level of symptom severity and/or impairment. Offspring with only mild episodes of MDD were counted as non-cases. Severity of MDD episodes in offspring was coded using the DSM-III-R/DSM-IV severity specifiers. Among offspring with a history of DSM-III-R MDD, the inter-rater reliability for the distinction between mild *versus* moderate, severe, or with psychotic features was $\kappa = 0{\cdot}46$ ($n = 213$).

The clinical features of depression in parents, derived using the best-estimate procedure, included: (1) severity of depressive symptoms, also assessed using the DSM-IV severity specifiers and coded as mild *versus* moderate, severe, or with psychotic features; (2) recurrent *versus* single episode; (3) chronic, defined as an episode lasting at least 2 years or a history of dysthymic disorder; and (4) age of onset, which, following Weissman *et al.* (1984), we dichotomized into $\leqslant 20$ years *versus* 21 years or older. The results were similar, but not quite as strong, using age 30 as the cut-off. Inter-rater reliability was $\kappa = 0{\cdot}81$ for severity; $\kappa = 0{\cdot}72$ for recurrent; $\kappa = 0{\cdot}57$ for chronic; and $\kappa = 0{\cdot}81$ for early-onset (n's ranged from 175–183).

For both offspring and parents, the following specific anxiety disorders were included in deriving the category of any anxiety disorder: panic disorder, agoraphobia without a history of panic disorder, social phobia, simple/specific phobia, obsessive–compulsive disorder, generalized anxiety disorder, post-traumatic stress disorder and anxiety disorder not otherwise specified. For offspring, diagnoses (assessed at T1 and T2 only) of separation anxiety disorder, overanxious disorder, and avoidant disorder of childhood/adolescence were also included. The following specific substance use disorders were included in the any substance use disorder category: alcohol abuse or dependence, sedative-hypnotic-anxiolytic abuse or dependence, cannabis abuse or dependence, stimulant abuse or dependence, opioid abuse or dependence, cocaine abuse or dependence, hallucinogen/PCP abuse or dependence, and polydrug dependence. For offspring and parents with multiple anxiety or substance use disorders, the age of onset was coded as the earliest condition in that group of disorders.

To ensure that the temporal direction of the associations between parental and offspring psychopathology was unambiguous, the onset of the disorders in the parent that were included as independent variables in any given analysis had to have preceded the onset of the disorder in their offspring that served as the dependent variable (if the offspring had experienced that disorder). In addition, we only considered parents to have a disorder if the onset was prior to the T1 assessment. If the parental disorder first appeared after the offspring had developed the disorder in the analysis or after the offspring entered the study at T1, it was considered absent. This is a conservative approach that should slightly attenuate the associations between parent and offspring psychopathology.

Data analysis

Caucasian OADP participants with no history of psychopathology through T2 were undersampled in the T3 follow-up, hence in all statistical analyses these offspring were assigned a weight of 2·05 reflecting their probability of being selected at T3. All participants with a history of psychopathology through T2 and all non-white participants were selected for the T2 assessment, hence were assigned a weight of

1·00. Although the analyses used weighted data, the numbers and proportions of participants presented in the tables are unweighted.

Rates of disorders in offspring were examined using Cox proportional hazards (PH) models. Offspring with diagnostic data on only one parent ($n=17$) were excluded from analyses requiring both parents. As we required that the onset of a disorder in the parent preceded the onset of that disorder in the offspring, the number of parents considered to have each disorder varied slightly depending on which disorder in offspring served as the dependent variable. Analyses were conducted using SUDAAN (Shah *et al.* 1997).

RESULTS

Characteristics of parents and offspring

The mean age of the offspring at T1 was 16·6 years (S.D. = 1·2); 41·7% were male, and 90·3% were white. At T1, 55·6% lived with both biological parents, 32·9% lived with their mother only, 7·8% lived with their father only, and 3·8% lived with neither biological parent. With respect to diagnoses through T3, 50·5% of the offspring had a lifetime MDD; 20·8% had a lifetime anxiety disorder; and 38·2% had a lifetime substance use disorder. The weighted lifetime prevalence of MDD in the sample was 42·1%.

The mean ages of the mothers and fathers at T1 were 40·7 years (S.D. = 5·1) and 42·5 years (S.D. = 6·4) respectively. In 43·5% of the families, at least one parent had a 4-year college degree. Of the mothers, 27·7% had a lifetime MDD, 14·3% had a lifetime anxiety disorder, and 19·1% had a lifetime substance use disorder. Of the fathers, 14·1% had a lifetime MDD, 7·0% had a lifetime anxiety disorder, and 43·4% had a lifetime substance use disorder. These rates only include parents with an onset before T1 and prior to the onset of MDD in their offspring. Parents with a disorder that onset after T1 or following the onset of MDD in their offspring were counted as non-affected.

MDD in offspring

We examined the effects of parental MDD on lifetime MDD through T3 in offspring in several stages. First, we examined the unadjusted or minimally adjusted effects of maternal and paternal MDD and selected covariates on offspring MDD (see Table 2). The covariates included offspring gender, intactness of the family (as indexed by whether the offspring was living with both biological parents at T1), whether one or more parent had completed college by T1 (serving as a proxy for socio-economic status), and maternal and paternal anxiety and substance use disorders. The analyses involving offspring gender, intactness of the family, and parental education were unadjusted; the analyses involving maternal and paternal MDD, anxiety disorder, and substance use disorder controlled for whether the parent had received a direct interview.

Female gender in offspring, a non-intact family, lower parental education, maternal MDD, maternal substance use disorder, and paternal substance use disorder were significantly associated with increased rates of MDD in offspring. In addition, there were non-significant trends for associations between paternal MDD ($p=0·065$) and maternal anxiety disorders ($p=0·08$) and offspring MDD.

Next, we examined the independent effects of maternal and paternal MDD on offspring MDD after controlling for offspring gender, parental education, intactness of the family, whether the parent had received a direct interview, and maternal and paternal anxiety and substance use disorders (see Table 2). Maternal, but not paternal, MDD was significantly associated with MDD in offspring. Maternal and paternal anxiety disorders and maternal substance use disorders did not make significant independent contributions to predicting offspring MDD. Paternal substance use disorders was associated with MDD in offspring at a trend level ($p=0·058$).

More offspring lived with their mothers than fathers, hence the stronger effect for maternal MDD may have been due to greater exposure to maternal depression. To test this, we examined a model that included offspring gender, the interview status of each parent, maternal MDD, paternal MDD, whether the offspring lived with their mother at T1, whether the offspring lived with their father at T1, and cross-product terms for the interactions between living with each parent at T1 and MDD in that parent. Neither of the interactions approached significance. In addition, a higher proportion of mothers than

Table 2. *Parental psychopathology and risk for offspring MDD (n = 775)*

Parental psychopathology and covariates	% (*n*)	Offspring MDD			
		Baseline model		Final model	
		HR	(95% CI)	HR	(95% CI)
Offspring sex					
Female	60·4 (273/452)	2·18**	(1·72–2·76)	2·10**	(1·69–2·79)
Male	36·5 (118/323)				
Live with both biological parents					
Yes	45·0 (193/429)	0·67**	(0·54–0·85)	0·82	(0·63–1·05)
No	57·4 (197/343)				
Parent completed college					
Yes	46·9 (152/324)	0·79*	(0·63–0·99)	0·86	(0·68–1·10)
No	53·3 (224/420)				
Maternal MDD					
Yes	61·9 (133/215)	1·74**	(1·38–2·20)	1·54**	(1·16–2·03)
No	46·1 (258/560)				
Paternal MDD					
Yes	57·0 (61/107)	1·36^{+}	(0·98–1·88)	1·11	(0·78–1·58)
No	49·6 (322/651)				
Maternal anxiety					
Yes	57·7 (64/111)	1·30^{+}	(0·97–1·75)	0·95	(0·67–1·34)
No	49·2 (327/664)				
Paternal anxiety					
Yes	52·8 (28/53)	1·30	(0·83–2·05)	1·17	(0·70–1·95)
No	50·4 (355/705)				
Maternal substance					
Yes	56·8 (84/148)	1·38*	(1·04–1·82)	1·02	(0·75–1·39)
No	48·9 (307/627)				
Paternal substance					
Yes	55·9 (184/329)	1·39*	(1·12–1·74)	1·26^{+}	(0·99–1·61)
No	46·4 (199/429)				

MDD, Major Depressive Disorder; HR, Hazard ratio; CI, confidence interval.

Baseline model refers to unadjusted associations for offspring gender, intact family at T1, and parental education at T1; associations adjusted for maternal interview status for maternal MDD, maternal anxiety disorder, and maternal substance abuse disorder; and associations adjusted for paternal interview status for paternal MDD, paternal anxiety disorder, and paternal substance abuse disorder. Final model refers to unique associations adjusted for maternal and paternal interview status and all other variables in the table. % (*n*) indicates the number and proportion of offspring at each level of the independent variable (or row) with MDD.

$^{+}$ $p < 0{\cdot}10$, * $p \leqslant 0{\cdot}05$, ** $p < 0{\cdot}01$.

fathers received direct interviews. To determine if this accounted for the stronger effects of maternal than paternal MDD, we tested a model that included offspring gender, the interview status of each parent, maternal MDD, paternal MDD, and cross-product terms for the interactions between maternal and paternal interview status with maternal and paternal MDD, respectively. Neither interaction was significant.†

Effect of a higher threshold for MDD in offspring

To examine the effects of raising the threshold for defining MDD caseness in offspring, we

† We also conducted several further analyses to explore the effects of gender and assortative mating. To explore whether the interaction between offspring and parent gender influenced rates of MDD in offspring, we tested a PH model that included main effects for maternal and paternal interview status, offspring gender, maternal MDD, paternal MDD, and cross-product terms for offspring gender × maternal MDD and offspring gender × paternal MDD. Neither interaction approached statistical significance. To explore whether paternal psychopathology moderated the association between maternal psychopathology and rates of MDD in offspring, we tested three PH models. In the first model, we entered maternal and paternal interview status, offspring gender, maternal MDD, paternal MDD, and a cross-product term for the interaction of maternal MDD × paternal MDD. This interaction did not approach significance. In the second model, we added five further variables: maternal anxiety disorders, paternal anxiety disorders, and cross-product terms for maternal MDD × paternal anxiety disorders, maternal anxiety disorders × paternal MDD, and maternal anxiety disorders × paternal anxiety disorders. None of the interactions approached significance. In the third model, we replaced the main effects and interaction terms involving maternal and paternal anxiety disorders in the previous model with the corresponding main effects and interaction terms for maternal and paternal substance use disorders. None of the interactions approached significance.

limited the MDD group to offspring with at least one lifetime episode of moderate or greater severity. Offspring with a history of only mild episodes of MDD were treated as non-cases, and combined with offspring with no history of MDD. Of the 392 offspring in the sample with a lifetime history of MDD, 291 (74·2%) had an episode rated as at least moderately severe. Using unweighted *n*'s, 47·4% (102/215) of the offspring of mothers with a history of MDD, and 33·7% (189/560) of offspring of mothers with no history of MDD had at least one episode of MDD of moderate or greater severity. Of offspring of fathers with a history of MDD, 52·3% (56/107) had an episode of MDD of moderate or greater severity compared to 35·3% (230/651) of offspring of fathers with no history of MDD.

When we repeated the series of analyses above examining the effects of parental MDD on offspring MDD using this more restrictive definition of caseness in offspring, the effects of paternal MDD on offspring MDD were stronger and statistically significant. In a multivariate model that included maternal and paternal interview status, offspring sex, socio-economic status, intact home, maternal and paternal anxiety and substance use disorders, and maternal MDD, paternal MDD was significantly associated with moderate to severe MDD in offspring [Hazard ratio (HR) 1·49, 95% confidence interval (CI) 1·03–2·14, $p=0·033$]. Maternal MDD also made a significant independent contribution (HR 1·42, 95% CI 1·04–1·95, $p=0·028$).

Anxiety and substance use disorders in offspring

A number of studies have also reported elevated rates of non-mood disorders in the offspring of depressed mothers and the offspring of combined samples of depressed mothers and fathers (Weissman *et al.* 1997; Beardslee *et al.* 1998; Goodman & Gotlib, 1999). In order to extend our analysis of the association between paternal MDD and offspring psychopathology, we examined the associations between maternal and paternal MDD and rates of anxiety and substance use disorders in offspring. These associations, adjusted for parental interview status, are presented in Table 3. Maternal MDD, but not paternal MDD, predicted a significantly higher rate of anxiety disorders in offspring. Neither maternal nor paternal MDD were associated with substance use disorders in offspring. In addition, maternal and paternal anxiety disorders predicted offspring anxiety disorders, and maternal and paternal substance use disorders were associated with substance use disorders in offspring.

As a more stringent test of the associations between maternal and paternal MDD and non-mood disorders in offspring, we examined two further PH models (see Table 3). The interview status of each parent, offspring gender, and maternal and paternal MDD were included in both models. The first model examined the associations between maternal and paternal MDD and anxiety disorders in offspring, and included maternal and paternal anxiety disorders as covariates. In this model, neither maternal MDD nor paternal MDD predicted anxiety disorders in offspring.

The second model examined the associations between maternal and paternal MDD and substance use disorders in offspring, and included maternal and paternal substance use disorders as covariates. Neither maternal MDD nor paternal MDD predicted substance use disorders in offspring.

Clinical characteristics of parental depression

Finally, we examined the associations between selected clinical characteristics of parental depression and rates of MDD in offspring. The analyses were conducted separately for depressed mothers and depressed fathers, and were limited to offspring with a depressed parent. Of the 215 depressed mothers in this set of analyses, 66 (30·7%) had an early onset, 145 (67·4%) had recurrent episodes, 67 (31·2%) had chronic episodes, and 184 (85·6%) had an episode of at least moderate severity. Of the 107 depressed fathers in this set of analyses, 26 (24·3%) had an early onset, 70 (65·4%) had recurrent episodes, 33 (30·8%) had chronic episodes, and 91 (85·0%) had an episode of at least moderate severity.

Offspring of depressed mothers and fathers with and without each clinical characteristic were compared using univariate PH models (see Table 4). Offspring of mothers with early-onset MDD, and offspring of fathers with early-onset MDD and recurrent MDD had significantly increased risks of MDD. In addition, there was

Table 3. *Parental psychopathology and risk for offspring anxiety disorders and substance abuse/dependence (n = 775)*

	Offspring anxiety					Offspring substance use				
		Partly adjusted		Fully adjusted			Partly adjusted		Fully adjusted	
Parent disorder	% (*n*)	HR	(95% CI)	HR	(95% CI)	% (*n*)	HR	(95% CI)	HR	(95% CI)
Maternal MDD										
Yes	25·0 (54/216)	1·45*	(1·02–2·05)	1·14	(0·77–1·70)	42·1 (91/221)	1·26	(0·96–1·65)	1·24	(0·93–1·66)
No	19·1 (107/559)					37·4 (205/554)				
Paternal MDD										
Yes	22·5 (25/111)	1·15	(0·74–1·79)	1·00	(0·64–1·57)	41·7 (48/115)	1·21	(0·86–1·70)	1·12	(0·78–1·59)
No	20·6 (133/647)					38·1 (242/643)				
Maternal anxiety										
Yes	27·9 (31/111)	1·62*	(1·05–2·48)	1·46	(0·89–2·38)					
No	19·6 (130/664)									
Paternal anxiety										
Yes	36·5 (19/52)	2·54**	(1·55–4·16)	2·44**	(1·50–3·96)					
No	19·7 (139/706)									
Maternal substance										
Yes						46·1 (70/152)	1·47*	(1·10–1·97)	1·34	(0·99–1·83)
No						36·3 (226/623)				
Paternal substance										
Yes						41·9 (139/331)	1·29*	(1·00–1·65)	1·20	(0·93–1·56)
No						35·4 (151/427)				

MDD, Major Depressive Disorder; HR, Hazard ratio; CI, confidence interval.

Partly adjusted refers to associations adjusted for maternal interview status or paternal interview status. Fully adjusted refers to associations adjusted for interview status of each parent, offspring gender, and all other variables in that column. % (*n*) indicates the number and proportion of offspring at each level of the independent variable (or row) with an anxiety or substance use disorder. Empty cells indicate that the variable was not included in the model (e.g. parental anxiety disorders were not included in the model for offspring substance use disorders, and parental substance use disorder were not included in the model for offspring anxiety disorders).

* $p < 0{\cdot}05$, ** $p < 0{\cdot}01$.

a trend for a higher rate of MDD in the offspring of mothers with chronic MDD. The effects for maternal recurrent MDD, paternal chronic MDD, and moderate to severe maternal and paternal MDD were not significant.

DISCUSSION

Many studies have demonstrated that the offspring of mothers with MDD are at increased risk for depression. Much less, however, is known about the association between paternal MDD and offspring depression. Using a large community sample of parents and their adolescent and young adult offspring, we replicated the finding that maternal MDD was significantly associated with MDD in offspring. In contrast, the association between paternal MDD and offspring MDD reached only a trend level of significance, and disappeared after controlling for maternal MDD and selected demographic covariates and parental non-mood disorders. However, when a more stringent threshold for defining MDD in offspring was employed, a significant association between paternal MDD and offspring depression was obtained, and we found that MDD in both mothers and fathers were independently associated with MDD in offspring. In addition, we found that early MDD onset in both mothers and fathers, and recurrent MDD in fathers were significantly associated with elevated rates of MDD in offspring.

We are aware of only two previous studies that used large community samples of depressed fathers as well as depressed mothers. Lieb *et al.* (2002) reported that maternal and paternal MDD were both associated with increased rates of MDD in offspring, whereas Brennan *et al.* (2002) found that maternal depression, but not paternal depression, was associated with depression in offspring. Our findings are partially consistent with both of these studies. Using DSM-III-R criteria for MDD in offspring, we

Table 4. *Maternal and paternal MDD clinical features and risk for offspring MDD*

	Offspring of depressed mothers				Offspring of depressed fathers			
Parental MDD feature	*n*	(% MDD)	HR	(95% CI)	*n*	(% MDD)	HR	(95% CI)
Early onset								
Yes	48/66	(72·7)	1·52*	(1·02–2·27)	21/26	(80·8)	2·48**	(1·38–4·46)
No	85/149	(57·0)			40/81	(49·4)		
Recurrent								
Yes	92/145	(63·4)	1·10	(0·73–1·64)	45/70	(64·3)	1·98*	(1·02–3·83)
No	41/70	(58·6)			16/37	(43·2)		
Moderate/severe								
Yes	113/184	(61·4)	0·96	(0·59–1·56)	52/91	(57·1)	1·02	(0·50–2·07)
No	20/31	(64·5)			9/16	(56·3)		
Chronic								
Yes	48/67	(71·6)	1·41^{+}	(0·97–2·05)	18/33	(54·5)	0·84	(0·44–1·57)
No	85/148	(57·4)			43/74	(58·1)		

Offspring of depressed mothers $n=215$; Offspring of depressed fathers $n=107$.
MDD, Major Depressive Disorder; HR, Hazard ratio; CI, confidence interval.
Columns labelled *n* reflect the number of offspring of parents with the MDD feature; % MDD reflects the proportion of offspring of parents with the MDD feature who have a lifetime history of MDD [e.g. of the 66 offspring of mothers with early-onset MDD, 48 (72·7%) had MDD].
$^{+}$ $p<0·10$, * $p<0·05$, ** $p<0·01$.

found that the association between parental MDD and offspring depression was limited to depressed mothers. However, when we raised the threshold to require at least one MDD episode of at least moderate severity in offspring, we also found a significant association between paternal MDD and offspring depression. These findings raise the possibility that conflicting results in studies comparing the effects of maternal and paternal depression may reflect implicit differences in the thresholds used to diagnose MDD in offspring, In addition, these results suggest that future studies should examine the data using several alternative approaches to case definition.

We examined several possible explanations for why there was an effect for maternal MDD, but not paternal MDD, in the primary analyses using DSM-III-R criteria for MDD in offspring. First, more mothers than fathers received direct interviews, and offspring's collateral reports of maternal MDD were somewhat more sensitive than reports of paternal MDD. Hence, it is conceivable that our findings are due to more accurate diagnoses of MDD in mothers than fathers. However, the significant associations for maternal, but not paternal, MDD remained evident after controlling for whether the parent was interviewed, and there was no evidence of interview status by parental diagnosis interactions. Second, offspring were more likely to reside with their mothers than fathers, and therefore, may have had greater exposure to maternal than paternal depression. While we did not assess the actual time spent with either parent during episodes of parental MDD, we did control for the effects of residing with both biological parents at T1 in the analyses. In addition, we examined interactions between residing with each parent and parental diagnoses of MDD, and did not obtain significant effects.

Our secondary analyses revealed significant associations between both maternal MDD and paternal MDD and MDD of at least moderate severity in offspring. Thus, it appears that the association between maternal MDD and offspring MDD is evident throughout the range of offspring severity, whereas the association with paternal MDD is limited to the more severe cases of depression in offspring. This has important implications for modeling the familial aggregation of MDD, as it suggests that the processes underlying the intergenerational transmission of depression in mothers and fathers may differ, at least to some extent.

We also examined whether maternal and paternal MDD were associated with increased rates of non-mood disorders in offspring. A number of previous studies have found elevated rates of anxiety and externalizing disorders in the offspring of depressed parents (Weissman *et al.* 1997; Beardslee *et al.* 1998; Goodman &

Gotlib, 1999). However, few previous studies have examined depressed mothers and fathers separately or controlled for the effects of non-mood disorders in the depressed parent and the co-parent. Consistent with the literature, we found that prior to adjusting for the effects of parental non-mood disorders, maternal MDD was significantly associated with an increased rate of anxiety disorders in offspring. However, after controlling for parental anxiety disorders, this association disappeared. These findings suggest that the elevated rates of non-mood disorders reported in previous studies of the offspring of depressed parents may be due to the direct transmission of these other disorders, rather than the effects of maternal MDD. Alternatively, the effects of maternal MDD on offspring anxiety disorders may be more easily detected in younger samples, as some cases of childhood anxiety disorders may subsequently evolve into depression and not be reported in assessments conducted in adolescence or young adulthood.

Early-onset (<21 years of age) MDD in both mothers and fathers was associated with a significantly increased risk of MDD in the offspring. In addition, the offspring of fathers with recurrent MDD exhibited an increased rate of MDD. These data are consistent with a number of twin (Kendler *et al.* 1999), family (Bland *et al.* 1986; Weissman *et al.* 1986), and offspring (Klein *et al.* 1988; Warner *et al.* 1995) studies indicating that early-onset and recurrent MDD are associated with greater familial aggregation. Most of this work has been based on samples of depressed mothers or combined samples of depressed mothers and fathers. Our findings indicate that the association between early-onset and recurrent MDD in parents and increased risk to offspring also applies to depressed fathers. Our design cannot tease apart genetic from environmental effects. Thus, we do not know whether early-onset MDD in the parent is associated with a greater genetic liability or whether offspring of parents with early-onset MDD are exposed to parental depression at an earlier age or for a longer period of time. Unfortunately, we did not have sufficiently detailed data on the course of parental depression and the periods in which the offspring was living with each parent to disentangle the effects of parental age of onset and recurrence from the timing and duration of exposure of offspring to parental MDD.

Our findings appear to be inconsistent with Hammen & Brennan's (2003) recent report that the severity of maternal depression was associated with risk for MDD in a large community sample of adolescents. However, an important difference is that our analyses were limited to parents with MDD, whereas Hammen & Brennan (2003) combined depressed and non-depressed mothers and used a four-point severity scale that included no depression, minor/subthreshold depression, mild/moderate MDD, and severe/psychotic MDD. Thus, it is unclear whether Hammen & Brennan's (2003) findings reflect differences between parents with mild/moderate *versus* severe/psychotic MDD or between the presence *versus* absence of parental MDD.

The magnitude of the significant associations between parental MDD and offspring psychopathology was generally in the small-to-medium range. This is consistent with the view that parental depression is only one of many factors contributing to the development of MDD in offspring (Goodman & Gotlib, 1999). However, due to the large sample and high prevalence of MDD, the confidence intervals were relatively narrow, indicating that the hazard ratios were estimated with a high degree of precision.

The lifetime prevalence of MDD through age 24 years in our sample of offspring (weighted prevalence = 42%) was considerably higher than other epidemiological studies of depression. For example, the estimated lifetime prevalence of MDD through age 24 years in the National Comorbidity Survey (NCS; Kessler & Walters, 1998) was 21%. However, most epidemiological studies are based on single-wave retrospective assessments of predominantly adult samples. In contrast, the prevalence of MDD in the OADP is based on three diagnostic evaluations conducted over a 7–8 years period from mid-adolescence to early adulthood. Interestingly, the shape of the age of onset functions for ages 15–24 years in the OADP and NCS are very similar, and both studies have relatively similar 12-month total incidence rates (7·6% and 6·6% respectively) and 12-month prevalence rates (9·9% and 12·4% respectively). This suggests that the higher lifetime prevalence in the OADP may be due to its prospective design and more

intensive surveillance. We suspect that this resulted in the OADP detecting a number of milder cases (e.g. less severe, shorter duration, single episode) that are not identified in single-wave retrospective designs covering a much broader time period.

This study had a number of strengths, including the use of a large community sample, assessments of both mothers and fathers using semi-structured diagnostic interviews, and repeated evaluations of offspring. However, the study also had a number of limitations. First, there are limits to the generalizability of the sample, as participants were predominantly Caucasian and only adolescents who were enrolled in high school were included in the T1 sampling frame.

Second, the possibility of sampling bias must be considered, as the participation rate at T1 was modest, and participants were more likely than non-participants to be female and to come from families with slightly higher socio-economic status.

Third, we were able to conduct direct interviews with only 75% of the mothers and 46% of the fathers. In order to minimize sampling bias, we chose to include parents who could not be personally interviewed and derived diagnoses for them using the family history method. However, the sensitivity of the family history method is limited, and informants' reports may be influenced by their own history of psychopathology (Kendler *et al.* 1991; Chapman *et al.* 1994). In order to increase the sensitivity of family history information and reduce the effects of informants' biases, we attempted to obtain data from two informants when a parent was unavailable for interview. In addition, we included interview status as a covariate in our analyses, and tested for interactions between interview status and parental MDD.

Fourth, the data on diagnoses and age of onset in parents and offspring were retrospective, although for the offspring this limitation was partially mitigated by multiple follow-up evaluations.

Fifth, the inter-rater reliability of some clinical features in parents and offspring was only moderate.

Sixth, we used a cohort of offspring who were followed from mid-late adolescence into early adulthood. Although this increased the homogeneity of the sample, the findings may differ for younger offspring. For example, in a recent meta-analysis, Connell & Goodman (2002) reported that the associations between maternal and paternal depression and offspring internalizing symptoms varied somewhat as a function of the children's age.

Seventh, we focused on psychiatric diagnoses in offspring. It is also important to compare the associations between maternal and paternal MDD and other domains of offspring functioning, such as interpersonal and academic/vocational adjustment. Finally, we did not attempt to examine the processes or mechanisms that underlie the intergenerational transmission of MDD in this paper. We intend to explore these issues in future reports.

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DECLARATION OF INTEREST

None.

REFERENCES

APA (1987). *Diagnostic and Statistical Manual of Mental Disorders* (3rd edn revised). American Psychiatric Press: Washington, DC.

APA (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th edn). American Psychiatric Press: Washington, DC.

Beardslee, W. R., Versage, E. M. & Gladstone, T. R. G. (1998). Children of affectively ill parents: a review of the past 10 years. *Journal of the American Academy of Child and Adolescent Psychiatry* **37**, 1134–1141.

Bland, R. C., Newman, S. C. & Orn, H. (1986). Recurrent and non-recurrent depression: A family study. *Archives of General Psychiatry* **43**, 1085–1089.

Brennan, P. A., Hammen, C., Katz, A. R. & Le Brocque, R. M. (2002). Maternal depression, paternal psychopathology, and adolescent diagnostic outcomes. *Journal of Consulting and Clinical Psychology* **70**, 1075–1085.

Chapman, T. F., Mannuzza, S., Klein, D. F. & Fyer, A. J. (1994). Effects of informant mental disorders on psychiatric family history data. *American Journal of Psychiatry* **151**, 574–579.

Cohen, P. R. (1988). The effects of instruments and informants on ascertainment. In *Relatives at Risk for Mental Disorders* (ed. D. L. Dunner, E. S. Gershon and J. E. Barrett), pp. 32–51. Raven Press: New York.

Connell, A. M. & Goodman, S. H. (2002). The association between psychopathology in fathers versus mothers and children's internalizing and externalizing behavior problems: a meta-analysis. *Psychological Bulletin* **128**, 746–773.

Costello, C. G. (1993). Psychopathology in the clinic and in the community. In *Basic issues in Psychopathology* (ed. C. G. Costello), pp. 67–102. Guilford Press: New York.

First, M. B., Spitzer, R. L., Gibbon, M. & Williams, J. B. W. (1996). *Structured Clinical Interview for DSM-IV Axis I Disorders, Non-Patient edition* (*SCID-NP, Version 2.0*). Biometrics Research Department, New York State Psychiatric Institute: New York.

Goodman, S. H. & Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: a developmental model for understanding mechanisms of transmission. *Psychological Review* **106**, 485–490.

Hammen, C. & Brennan, P. A. (2003). Severity, chronicity, and timing of maternal depression and risk for adolescent offspring diagnoses in a community sample. *Archives of General Psychiatry* **60**, 253–258.

Keller, M. B., Beardslee, W. R., Dorer, D. J., Lavori, P. W., Samuelson, H. & Klerman, G. R. (1986). Impact of severity and chronicity of parental affective illness on adaptive functioning and psychopathology in children. *Archives of General Psychiatry* **43**, 930–937.

Keller, M. B., Lavori, P. W., Friedman, B., Nielsen, E., Endicott, J. & McDonald-Scott, P. A. (1987). The Longitudinal Interval Follow-up Evaluation: a comprehensive method for assessing outcome in prospective longitudinal studies. *Archives of General Psychiatry* **44**, 540–548.

Kendler, K. S., Gardner, C. O. & Prescott, C. A. (1999). Clinical characteristics of major depression that predict risk of depression in relatives. *Archives of General Psychiatry* **56**, 322–327.

Kendler, K. S., Silberg, J. L., Neale, M. C., Kessler, R. C., Heath, A. C. & Eaves, L. J. (1991). The family history method: whose psychiatric history is measured? *American Journal of Psychiatry* **148**, 1501–1504.

Kessler, R. C. & Walters, E. E. (1998). Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the National Comorbidity Survey. *Depression and Anxiety* **7**, 3–14.

Klein, D. N., Clark, D. C., Dansky, L. & Margolis, E. T. (1988). Dysthymia in the offspring of parents with primary unipolar affective disorder. *Journal of Abnormal Psychology* **97**, 265–274.

Klein, D. N., Lewinsohn, P. M., Rohde, P., Seeley, J. R. & Durbin, E. C. (2002). Clinical features of major depressive disorder in adolescents and their relatives: Impact on familial aggregation, implications for phenotype definition, and specificity of transmission. *Journal of Abnormal Psychology* **111**, 98–106.

Klein, D. N., Lewinsohn, P. M., Seeley, J. R. & Rohde, P. (2001). Family study of major depressive disorder in a community sample of adolescents. *Archives of General Psychiatry* **58**, 13–20.

Klein, D. N., Ouimette, P. C., Kelly, H. S., Ferro, T. & Riso, L. P. (1994). Test-retest reliability of team consensus best-estimate diagnoses of Axis I and II disorders in a family study. *American Journal of Psychiatry* **151**, 1043–1047.

Leckman, J. F., Sholomskas, D., Thompson, D., Belanger, A. & Weissman, M. M. (1982). Best estimate of lifetime psychiatric diagnosis: a methodological study. *Archives of General Psychiatry* **39**, 879–883.

Lewinsohn, P. M., Hops, H., Roberts, R. E., Seeley, J. R. & Andrews, J. A. (1993). Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *Journal of Abnormal Psychology* **102**, 133–144.

Lieb, R., Isensee, B., Hofler, M., Pfister, H. & Wittchen, H.-U. (2002). Parental major depression and the risk of depression and other mental disorders in offspring: a prospective-longitudinal community study. *Archives of General Psychiatry* **59**, 365–374.

Mannuzza, S. & Fyer, A. J. (1990). *Family Informant Schedule and Criteria* (*FISC*), (July 1990 revision). Anxiety Disorders Clinic, New York State Psychiatric Institute: New York.

Moeller-Leimkuehler, A. M. (2002). Barriers to help-seeking by men: a review of sociocultural and clinical literature with particular reference to depression. *Journal of Affective Disorders* **71**, 1–9.

Nomura, Y., Warner, V. & Wickramaratne, P. (2001). Parents concordant for major depressive disorder and the effect of psychopathology in offspring. *Psychological Medicine* **31**, 1211–1222.

Orvaschel, H., Puig-Antich, J., Chambers, W. J., Tabrizi, M. A. & Johnson, R. (1982). Retrospective assessment of prepubertal major depression with the Kiddie-SADS-E. *Journal of the American Academy of Child and Adolescent Psychiatry* **21**, 392–397.

Orvaschel, H., Walsh-Allis, G. & Ye, W. (1988). Psychopathology in children of parents with recurrent depression. *Journal of Abnormal Child Psychology* **16**, 17–28.

Phares, V. (2002). Family context: fathers and other supports. In *Children of Depressed Parents: Mechanisms of Risk and Implications for Treatment* (ed. S. H. Goodman and I. H. Gotlib), pp. 203–225. American Psychological Association: Washington, DC.

Rohde, P., Lewinsohn, P. M. & Seeley, J. R. (1997). Comparability of telephone and face-to-face interviews assessing Axis I and II disorders. *American Journal of Psychiatry* **154**, 1593–1598.

Shah, B. V., Barnwell, B. G. & Biegler, G. S. (1997). *SUDAAN User's Manual, release 7.5*. Research Triangle Institute: Research Triangle Park, NC.

Sobin, E., Weissman, M. M., Goldstein, R. B., Adams, P., Wickramaratne, P., Warner, V. & Lish, J. D. (1993). Diagnostic interviewing for family studies: comparing telephone and face-to-face methods for the diagnosis of lifetime psychiatric disorders. *Psychiatric Genetics* **3**, 227–233.

Warner, V., Mufson, L., Weissman, M. M. (1995). Offspring at high and low risk for depression and anxiety: Mechanisms of psychiatric disorder. *Journal of the American Academy of Child and Adolescent Psychiatry* **34**, 786–797.

Weissman, M. M., Merikangas, K. R., Wickramaratne, P., Kidd, K. K., Prusoff, B. A., Leckman, J. F. & Pauls, D. L. (1986). Understanding the clinical heterogeneity of major depression using family data. *Archives of General Psychiatry* **43**, 430–434.

Weissman, M. M., Warner, V., Wickramaratne, P., Moreau, D. & Olfson, M. (1997). Offspring of depressed parents: 10 years later. *Archives of General Psychiatry* **54**, 932–940.

Weissman, M. M., Wickramaratne, P., Merikangas, K. R., Leckman, J. F., Prusoff, B. A., Caruso, K. A., Kidd, K. K. & Gammon, G. D. (1984). Onset of major depression in early adulthood: increased familial loading and specificity. *Archives of General Psychiatry* **41**, 1136–1143.