Remissions in Maternal Depression and Child Psychopathology
A STAR*D-Child Report

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Context  Children of depressed parents have high rates of anxiety, disruptive, and depressive disorders that begin early, often continue into adulthood, and are impairing.

Objective  To determine whether effective treatment with medication of women with major depression is associated with reduction of symptoms and diagnoses in their children.

Design  Assessments of children whose depressed mothers were being treated with medication as part of the multicenter Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial conducted (between December 16, 2001 and April 24, 2004) in broadly representative primary and psychiatric outpatient practices. Children were assessed by a team of evaluators not involved in maternal treatment and unaware of maternal outcomes. Study is ongoing with cases followed at 3-month intervals.

Setting and Patients  One hundred fifty-one mother-child pairs in 8 primary care and 11 psychiatric outpatient clinics across 7 regional centers in the United States. Children were aged 7 to 17 years.

Main Outcome Measures  Child diagnoses based on the Kiddie Schedule for Affective Disorders and Schizophrenia; child symptoms based on the Child Behavior Checklist; child functioning based on the Child Global Assessment Scale in mothers whose depression with treatment remitted with a score of 7 or lower or whose depression did not remit with a score higher than 7 on the Hamilton Rating Scale for Depression.

Results  Remission of maternal depression after 3 months of medication treatment was significantly associated with reductions in the children’s diagnoses and symptoms. There was an overall 11% decrease in rates of diagnoses in children of mothers whose depression remitted compared with an approximate 8% increase in rates of diagnoses in children of mothers whose depression did not. This rate difference remained statistically significant after controlling for the child’s age and sex, and possible confounding factors (P = .01). Of the children with a diagnosis at baseline, remission was reported in 33% of those whose mothers’ depression remitted compared with only a 12% remission rate among children of mothers whose depression did not remit. All children of mothers whose depression remitted after treatment and who themselves had no baseline diagnosis for depression remained free of psychiatric diagnoses at 3 months, whereas 17% of the children whose mothers remained depressed acquired a diagnosis. Findings were similar using child symptoms as an outcome. Greater level of maternal response was associated with fewer current diagnoses and symptoms in the children, and a maternal response of at least 50% was required to detect an improvement in the child.

Conclusions  Remission of maternal depression has a positive effect on both mothers and their children, whereas mothers who remain depressed may increase the rates of their children’s disorders. These findings support the importance of vigorous treatment for depressed mothers in primary care or psychiatric clinics and suggest the utility of evaluating the children, especially children whose mothers continue to be depressed.

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1389
ruptured parent-child attachment and poor parent-child bonding, may mediate the impact of parental depression on children's symptoms.7,8

Only a few studies of children of depressed parents have suggested some benefit for children of reducing parental symptoms, but none of those published have directly treated parental depression in a definitive large sample.9,10

One ongoing study of 129 high-risk offspring, aged 7 to 17 years, found that remission of depression in parents after 4 months of various treatments was associated with significant reductions in children's depressive, internalizing, and externalizing symptoms (J.G., PhD, oral communication, September 2005).

The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial provided a unique opportunity to study the children of ambulatory depressed mothers who were being treated and followed up as part of the study protocol.11-13 Our study was restricted to mothers because the rate of depression is higher in women than it is in men, particularly women in the child-rearing ages and because mothers are more likely than fathers to bring their children in for assessments. We previously reported the demographic and clinical characteristics of the mother-child pairs before the commencement of maternal treatment.14 Our focus herein is on the symptomatic and behavioral functioning of the children assessed 3 months after the initiation of treatment of maternal depression by a team of evaluators not involved in maternal treatment and unaware of maternal outcomes. These children will be followed up periodically for a year after maternal depression remission or for 2 years should the mother remain depressed. We hypothesized that reduction of maternal depression would be associated with reductions in current psychopathological symptoms and disorders in their offspring.

METHODS

The sample consisted of 151 mothers who were enrolled (recruited between December 16, 2001 and April 24, 2004) in STAR*D, a multisite US study designed to determine the comparative effectiveness and acceptability of different treatment options for a broadly representative group of outpatients with nonpsychotic major depressive disorder. The rationale, methods, and design of the trial have been detailed elsewhere.11-13 Clinical sites included primary care and outpatient psychiatric care settings serving public- or private-sector patients. Participants were adults, aged 18 to 75 years, with nonpsychotic major depressive disorder (baseline score on the 17-item Hamilton Rating Scale for Depression15,16 [HRSD] ≥14) and without a lifetime diagnosis of bipolar disorder, schizophrenia, or schizoaffective disorders. Patients with concurrent medical and psychiatric conditions, except as noted above, were included unless a medical condition contraindicated one of the study medications. The STAR*D trial offered 5 treatment levels delivered sequentially. At the outset, all study participants were initially treated with citalopram (level 1 treatment). Those not remitting with or intolerant of citalopram could receive subsequent treatment steps provided in an equiprobable randomized design described elsewhere.17

Because the STAR*D-Child study was an ancillary study and required separate scientific review, it was initiated about a year after the adult segment began. Seven of the 14 regional centers involved in the trial participated in the trial, based on willingness to participate, the presence of a substantial number of women in the child-rearing ages, and the availability of clinicians experienced at evaluating children. Participating women aged 25 to 60 years were screened to ascertain whether they had children who met eligibility criteria. Eligible children had to be 7 through 17 years of age and living with their mothers (or in case of marital separation or divorce, living with her at least 50% of the time). Although participating children did not receive treatment, those who were receiving treatment elsewhere were not excluded from the study. If a mother had more than one child aged 7 through 17 years, one child was selected using a table of random numbers. Study is ongoing with cases followed at 3-month intervals. The STAR*D-Child protocol was reviewed and approved by the institutional review boards at each participating site. Written informed consent was obtained for both mothers and children.

Maternal Assessments

Mothers received a comprehensive battery of assessments as part of the adult portion of the study,11-13 which included baseline demographics, psychosocial and clinical features, and diagnostic and symptomatic status over time. Information on race and ethnicity was collected as part of the demographic assessment, and mothers selected their response from a list of provided categories.

The mother's initial diagnosis was established by clinical interview and confirmed using a symptom checklist based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV).13 The severity of depressive symptoms was estimated using the HRSD.15,16 Maternal remission was defined as an HRSD score of 7 or less, and response was defined as a 50% or greater reduction of the baseline HRSD score. Remission and response were also assessed by self-report, using the 16-item Quick Inventory of Depressive Symptomatology-Self Report.18-21 Because the findings between the 2 screening tools were similar, we report only the latter (Data for the Quick Inventory of Depressive Symptomatology-Self Report is available on request). Clinicians assessing maternal remission were independent of the clinicians assessing child outcomes.

Child Assessments

Children's psychiatric disorders at baseline and the 3-month evaluation were established by direct interview of mothers and children using the Kiddie Schedule for Affective Disorders and Schizophrenia—Present and Lifetime Version,22 a widely used valid and re-

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liable diagnostic assessment that generates DSM-IV diagnoses. To reduce participants’ burden, we selected sections of the Kiddie Schedule for Disorders and Schizophrenia that target disorders (affective, anxiety, and disruptive behavior disorder) known to be highly prevalent among children of depressed parents.23,25

The parent version of the Child Behavior Checklist (CBCL)23 was used to assess children’s symptoms, and the clinician-rated Child Global Assessment Scale (C-GAS)26 was used to assess child global functioning. The CBCL was administered to mothers to assess child social functioning in 3 domains—activities, socialization, and school functioning—and to assess symptoms associated with behavioral and emotional disorders. These symptoms are classified as internalizing (predominantly symptoms associated with anxiety and mood disorders), and externalizing (predominantly symptoms associated with disruptive behavior) disorders. Scores are presented as T scores ranging from 0 to 100, for which higher competency scores indicate superior social functioning (scores <30 are considered in the clinically impaired range), and higher psychopathology scores indicate a greater number or severity of symptoms (scores <70 are considered indicative of clinical impairment).

Overall child functioning was assessed using the C-GAS, by the same clinical interviewer that assessed the Kiddie Schedule for Disorders and Schizophrenia. The scale ranges from 0 to 100; scores higher than 90 are indicative of superior functioning, and scores lower than 70 indicate clinical impairment.

**Statistical Analyses**

Two main outcome measures were analyzed: change in overall rates of children’s diagnoses from baseline to 3 months and change in CBCL-scores from baseline to 3 months.

Changes in rates of child diagnoses from baseline to 3 months as a function of mother’s remission and subsequently mother’s level of response were analyzed using a repeated measures analysis with binary response data, using generalized estimating equation (GEE) methods.27 A linear probability model with an identity link function (rather than a logit-link function) was used to model interactions on the additive scale28 and to model a dose-response function using rates (rather than odds) as the outcome measure because we considered risk differences to be a more relevant measure than odds ratios in our study. The outcome measures in these models were the rates of diagnoses at each of the 2 time points, whereas the independent variables were time, mother’s remission or response level, and a time by mother’s remission or response level interaction term. Analyses were adjusted for age and sex of child, severity of maternal baseline symptoms, annual household income, mother’s treatment setting (primary vs psychiatric outpatient care), and treatment status of child during 3-month follow-up. Household income was selected as a priori as the primary marker for socioeconomic status; however, the results were unchanged when the mother’s educational level or when both income and educational level were included in the model. The interaction term of time × mother’s remission status was included to formally test whether changes in rates of childhood diagnoses differed significantly between mothers whose depression remitted and mothers whose depression remained. In the analysis of child’s diagnosis as a function of mother’s response level, the interaction term of time × mother’s response level was included to formally test whether the change in rate of diagnosis over time varied with the mother’s response level.

The relationship between maternal remission and changes in child’s outcome at 3 months, for children with and without diagnoses, was analyzed using separate logistic regression analyses with the outcome measure being remission for children with a baseline diagnosis and incidence or relapse for children without a baseline diagnosis, respectively. Analyses were adjusted for age and sex of the child, as well as the control variables listed above. Trends in rates of child diagnoses by mother’s response level in children with a baseline diagnosis and in rates of incidence or relapse in children without a baseline diagnosis were examined separately using the Cochran-Armitage test for trend.29 Low event rates precluded fitting regression models adjusting for potential confounders, such as age and sex of child, using generalized linear models with an identity-link function, to estimate parameters for adjusted trends.

Analyses of CBCL change scores were conducted using linear regression analysis. Specifically, the relation of mother’s remission status to change in CBCL score was modeled so that the change score was treated as the dependent variable, with mother’s remission status as a dichotomous independent variable, and with the baseline value of the CBCL score and the mother’s baseline HRDS as covariates. We also included the child’s age and sex in the model to control for potential confounding. Change scores rather than the 3-month score was used as the outcome measure for ease of interpretation. It has been shown that inferences resulting from this analysis are virtually identical no matter which of these outcome measures is used.30 In addition to the covariates previously noted, the regression analysis was repeated to include annual household income, mother’s treatment setting (primary vs psychiatric outpatient care), and treatment status of child during the 3-month follow-up period in order to investigate the further potential confounding effects of these variables. All statistical analyses were conducted using SAS statistical software version 9.0 (SAS Institute Inc, Cary, NC). P < .05 was considered statistically significant.

Six of the 114 mothers who received both baseline and 3-month follow-up assessments were missing follow-up HRDS scores. Scores for these mothers were imputed from the

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Quick Inventory of Depressive Symptomatology-Self Report, using an item-response theory analysis of the relation between the HRSD and the Quick Inventory of Depressive Symptomatology-Self Report scales, as used by the STAR*D study. Sensitivity analyses confirmed that the findings did not vary based on inclusion or exclusion of these 6 mothers.

### RESULTS

Eight hundred twenty-four women aged 25 through 60 years were recruited at 8 primary care and 11 psychiatric outpatient clinics across the 7 participating regional centers (Figure 1). Eight hundred eight (98%) of 824 women were screened to ascertain whether they had at least 1 child aged 7 through 17 years; only 177 (22%) of 808 had children in that age range; 151 (85%) of 177 eligible mother-child pairs consented to participate in the child study. One hundred fourteen (75%) of 151 of the mother-child pairs who received baseline assessments remained in the study at the time of their child’s 3-month assessment. Mothers who dropped out were not significantly different at baseline from mothers who remained in the study on demographics, or clinical characteristics, except that mother-child pairs were more likely to drop out of the study if the participating child was male than if the child was female (70% vs 30%, \( P = .01 \)). No differences were found among their children on baseline diagnoses, current or lifetime, severity of internalizing and externalizing symptoms, or functioning (data available on request).

### Remission of Maternal Depression

Of the mothers who received follow-up assessments, 38/114 (33%) met remission criteria before the 3-month follow-up assessment. The average (SD) time to remission was 55 (40) days. The overall response rate was 47% (54/114). Of the 38 mothers whose depression remitted, 35 (92%) did so while taking citalopram only (level 1 treatment). Two mothers’ medications were switched to extended release venlafaxine-XR, and one mother received a combination regimen of citalopram and bupropion, prior to remission. Table 1 and Table 2 summarize the baseline characteristics of mothers and their children. Mothers whose depression remained were financially poorer, more often receiving public assistance, and less likely to hold a college degree. They also had more severe baseline depression and comorbid anxiety but did not differ on age of onset or number of major depressive episodes. There were no significant differences on any of the child demographics or baseline clinical characteristics by mothers’ remission status.

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**Table 1. Baseline Characteristics of Depressed Mothers by Remission**

<table>
<thead>
<tr>
<th>Maternal Characteristics</th>
<th>Remission (n = 38)</th>
<th>No Remission (n = 76)</th>
<th>( P ) Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>11 (29)</td>
<td>34 (45)</td>
<td>.17</td>
</tr>
<tr>
<td>White</td>
<td>16 (42)</td>
<td>29 (39)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>7 (18)</td>
<td>11 (14)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4 (11)</td>
<td>2 (6)</td>
<td></td>
</tr>
<tr>
<td>Education, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; High school</td>
<td>3 (8)</td>
<td>11 (14)</td>
<td>.003</td>
</tr>
<tr>
<td>High school - &lt; college</td>
<td>18 (48)</td>
<td>53 (70)</td>
<td></td>
</tr>
<tr>
<td>≥ College</td>
<td>17 (44)</td>
<td>12 (16)</td>
<td></td>
</tr>
<tr>
<td>Annual household income, No. (%), $</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 15,000</td>
<td>4 (11)</td>
<td>22 (31)</td>
<td>.01</td>
</tr>
<tr>
<td>15,000-40,000</td>
<td>13 (36)</td>
<td>31 (43)</td>
<td></td>
</tr>
<tr>
<td>&gt; 40,000</td>
<td>19 (53)</td>
<td>19 (26)</td>
<td></td>
</tr>
<tr>
<td>Receiving public assistance</td>
<td>5 (13)</td>
<td>27 (36)</td>
<td>.01</td>
</tr>
<tr>
<td>Marital status, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Currently married</td>
<td>5 (13)</td>
<td>12 (16)</td>
<td>.79</td>
</tr>
<tr>
<td>Separated, divorced, or widowed</td>
<td>31 (82)</td>
<td>58 (76)</td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>2 (5)</td>
<td>6 (8)</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>38.6 (7.1)</td>
<td>37.8 (6.4)</td>
<td>.59</td>
</tr>
</tbody>
</table>

**Clinical history, mean (SD)**

| Baseline Hamilton Rating Scale for Depression score | 22.8 (4.1) | 25.3 (5.3) \( P = .01 \) |
| Age at first onset, y | 23 (12.3) | 19 (9.3) \( P = .13 \) |
| No. of major depressive episodes | 4 (9.0) | 9 (17.8) \( P = .19 \) |

**Comorbid Axis I diagnoses, No. (%)\(^†\)**

| Generalized anxiety disorder | 5 (13) | 23 (31) \( P = .04 \) |
| Obsessive-compulsive disorder | 3 (8) | 19 (25) \( P = .03 \) |
| Panic disorder               | 1 (2)  | 10 (13) \( P = .098 \) |
| Posttraumatic stress disorder | 4 (10) | 16 (21) \( P = .17 \) |
| Social phobia                | 17 (45) | 34 (45) \( P = .95 \) |
| Substance use disorder       | 3 (8)  | 10 (13) \( P = .41 \) |

**Treatment setting**

| Primary care | 19 (50) | 50 (65) \( P = .10 \) |
| Psychiatric  | 19 (50) | 26 (34) |

\( * \) The numbers in each category may vary due to missing data.

\( † \) Diagnoses based on the Psychiatric Diagnostic Screening Questionnaire.

\( ‡ \) Fisher exact test.

**Figure 1. Study Flow Diagram**

- 824 Women Aged 25 to 62 y Recruited at 7 Sites Participating in STAR*D-Child
- 808 Screened
- 177 Had Children Aged 7 to 17 y
- 151 Mother-Child Pairs Consented and Received Baseline Assessment
- 37 Pairs Did Not Complete 3-mo Assessment
- 114 Pairs Completed Child's 3-mo Assessment

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Relation of Maternal Remission to Changes in Rates of Child Diagnoses

As shown in Table 3, there was an overall 11% decrease in rates of diagnoses (from 35% [12/34] to 24% [8/34]) in children of remitted mothers vs an 8% increase (from 35% [25/71] to 43% [30/71]) in children of mothers with continuing depression. After controlling for the child’s age and sex, the change in rates was statistically significant for children of mothers whose depression remitted (12.3% decrease; 95% confidence interval [CI], 0.08%-23.8%; \( P = .03 \)) but not for children whose mother’s depression remained (6.5% increase; 95% CI, −2.5% to 15.4%; \( P = .15 \)). Formal tests to determine if the above rates of changes in children’s diagnoses varied with mothers’ remission status were statistically significant (\( P = .02 \)), and remained significant after further adjusting for maternal depression severity at baseline, maternal treatment setting, annual household income, and child treatment status during the 3-month follow-up interval (\( P = .01 \)).

The relation of maternal remission to child outcomes was also examined separately among children with and without a diagnosis at baseline. Thirty-seven offspring had psychiatric diagnoses at baseline. Of those whose mother’s depression remitted, one third (4/12) of the children’s own diagnoses had remitted, whereas only 12% (3/25) of the children of women whose depression remained lost their diagnosis, although this difference was not statistically significant (\( P = .21 \); Table 3).

Sixty-eight children had no psychiatric disorder at baseline. Of these children, all remained free of psychiatric disorders at the 3-month follow-up if the maternal depression remitted, whereas 17% (8/46) of children of mothers who remained depressed had an onset or relapse over this period (\( P = .05 \); Table 3). The higher rates of onset at 3 months among children of mothers whose depression remained were not associated with variation in lifetime rates of child disorders (\( P = .85 \)).

Figure 2 shows the pattern of change across the 3 months, for specific child disorders as well as for any disorder, by maternal remission status. Children whose mothers’ depression had remitted showed a decrease in the rates of depressive (18% [6/34] to 9% [3/34])

### Table 3: Relation Between Maternal Remission Status and Change in Any Child Diagnoses, Baseline to 3 Months*

<table>
<thead>
<tr>
<th>Maternal Remission Status</th>
<th>No. (%)</th>
<th>Rates of Current Child Diagnoses at Baseline and at 3 Months by Maternal Remission Status</th>
<th>Adjusted Rate Difference, % (95% CI)†</th>
<th>( P ) Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Remitted (n = 34)</strong></td>
<td></td>
<td>12 (35)</td>
<td>8 (24)</td>
<td>−12.3 (0.08 to 23.8)</td>
</tr>
<tr>
<td>Unremitted (n = 71)</td>
<td></td>
<td>25 (35)</td>
<td>30 (43)</td>
<td>+6.5 (−2.5 to 15.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maternal Remission Status by Child’s Diagnostic Status at 3 Months in Children With a Baseline Diagnosis</th>
<th>No. (%)</th>
<th>( P ) Value§</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Present</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remitted (n = 12)</td>
<td>8 (67)</td>
<td>.21‡</td>
</tr>
<tr>
<td>Unremitted (n = 25)</td>
<td>22 (88)</td>
<td></td>
</tr>
<tr>
<td><strong>Absent</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remitted (n = 22)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Unremitted (n = 46)</td>
<td>22 (100)</td>
<td>.05∥</td>
</tr>
</tbody>
</table>

*Numbers may vary in each category due to missing data.  
†Adjusting for child age and sex.  
‡Based on the Child-Global Assessment Scale. Higher scores indicate greater global functioning.  
§By \( \chi^2 \) test.  
∥\( P \) value based on Fisher exact test.

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and disruptive behavior disorders (18% [6/34] to 12% [4/34]) but with no change in anxiety disorders (4/34). In contrast, among children of mothers who did not remit, there was an increase in the rates of depressive (7% [5/71] to 11% [8/71]), anxiety (17% [13/71] to 25% [18/71]) and disruptive behavior (20% [15/71] to 24% [17/71]) disorders. Although the small sample size precluded statistical analysis on each disorder individually, the changes in rates of diagnoses between children of mothers whose depression did or did not remit were significantly different for the class of internalizing (including depressive or anxiety disorders; \( P = .03 \)) but not externalizing (disruptive behavior) disorders.

To ascertain whether maternal depression status biased reports of children’s psychopathology, we compared Kiddie Schedule for Disorders and Schizophrenia assessments of each mother and child (data available on request). There were no clinically or statistically significant differences between maternal and child reports of depressive or anxiety symptoms. In the case of disruptive behavior disorders, mothers tended to report more symptoms than their children, which is consistent with previous findings that parents are more likely to report behavior and conduct problems in their children than the children themselves.\(^{33,34}\) The difference between maternal and child reports did not vary significantly by maternal remission status.

Relation of Maternal Remission to Change in Child Symptoms
Changes in severity of children’s internalizing and externalizing symptoms over the 3-month period were also examined using changes in CBCL scores. After controlling for the child’s age and sex and adjusting for baseline severity of child and maternal symptoms, there was a significantly larger decrease in internalizing (adjusted mean score difference, 8.6; \( P < .001 \)), externalizing (6.6; \( P = .004 \)), and total (8.7; \( P < .001 \)) symptoms among children of mothers who had a remission from major depressive disorder over the 3-month period than among children of mothers whose major depressive disorder did not remit (TABLE 4). The above association between maternal remission and child symptoms remained significant after further adjusting for potential confounders including maternal socioeconomic status, maternal treatment setting, occurrence of stressful life events within the assessment interval, and the presence of a father in the household.

There were no significant changes in child functioning over the same period by maternal remission status, regardless of whether child functioning was assessed using the maternal-rated CBCL or the clinician-rated C-GAS (data available on request).

Relation of Level of Maternal Response to Change in Child Diagnoses and Symptoms
To quantify the magnitude of maternal improvement necessary to detect an appreciable improvement in the child, changes in child symptoms and diagnoses over the 3-month period were as-

### Table 4. Relation Between Maternal Remission Status and Change in Child Symptoms (Baseline to 3 Months)

<table>
<thead>
<tr>
<th>Child Outcomes</th>
<th>Baseline</th>
<th>Remitted†</th>
<th>Unremitted‡</th>
<th>Adjusted Mean Difference (CI)(\delta)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBCL psychopathology T scores*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internalizing</td>
<td>56.5 (11)</td>
<td>-11.6 (11)</td>
<td>-0.5 (12)</td>
<td>-8.6 (-4.8 to -12.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Externalizing</td>
<td>55.5 (12)</td>
<td>-9.9 (9)</td>
<td>-0.4 (11)</td>
<td>-6.6 (-2.4 to -10.8)</td>
<td>.004</td>
</tr>
<tr>
<td>Total</td>
<td>56.1 (11)</td>
<td>-12.5 (11)</td>
<td>-0.75 (13)</td>
<td>-8.7 (-4.2 to -13.2)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviation: CBCL, Child Behavior Checklist.

*The scoring range is from 0 to 100. Lower scores indicate superior functioning. Scores higher than 70 indicate clinical impairment.

†Hamilton Rating Scale for Depression, a 17-item questionnaire, score of 7 or lower closest evaluation prior to child’s 3-month assessment.
‡Hamilton Rating Scale for Depression score higher than 7 at closest evaluation prior to child’s 3-month assessment.
\(\delta\)Multiple linear regression, with CBCL score at the 3-month assessment as the outcome variable, maternal remission as a dichotomous independent variable, the child’s baseline symptom severity (CBCL score) and maternal baseline Hamilton Rating Scale for Depression score, as covariates, and the child’s age and sex as control variables.
sessed against the percentage change in maternal depressive symptoms. Maternal response was classified in 1 of 5 levels, based on the percent reduction in baseline HRSD scores: <0% (12 mothers), 0% to 24% (16 mothers), 25% to 49% (33 mothers), and 50% to 74% (27 mothers), 75% to 100% (26 mothers).

As shown in Figure 3A, the change in rates of child diagnoses over the 3 months was inversely related to the magnitude of the mother’s response level. However, at least 50% maternal response was required to discern improvement in the children. Specifically, children of mothers with 50% or greater reduction in depression severity had lower overall rates of diagnoses at the 3-month assessment (4% if maternal response was between 50% and 75%; 9% if maternal response exceeded 75%). In contrast, reduction in maternal depression less than 50% was associated with an increase in the rates of child diagnoses (13% if maternal response was <25%, and 18% if the mothers got worse). After controlling for the child’s age and sex, a significant linear relation was found between maternal response level and change in rates of child diagnoses (P = .04). When examined separately in children with and without a diagnosis at baseline, the level of maternal response was associated with onset or relapse of a child disorder (P = .002) but not with the child’s remission.

Similar results were obtained on the Child Behavior Checklist for internalizing (Figure 3B) and externalizing (Figure 3C) symptoms. Greater maternal response was associated with a greater decrease in both internalizing (adjusted mean difference, −3.4; P < .001) and externalizing (−3.7; P < .001) symptoms in the children, when tested in a linear regression model controlling for child age, sex, and severity of symptoms at baseline, as well as maternal baseline HRSD and household income.

**Effects of Treatment in Children**

We did not exclude children receiving treatment previously or after the baseline assessment. Only 28 children had received treatment for an emotional problem prior their mothers’ participation in the trial. The children who improved by their 3-month evaluation did not differ significantly from those who did not on lifetime diagnoses or treatment history, indicating that differential rates of improvement were unlikely attributable to lifetime course of illness.

We also examined whether the 12 children who received outpatient treatment during the 3 months differed from those who did not. There were no differences in severity of internalizing or externalizing symptoms at baseline between children who received treatment during the 3 months and those who did not. Children receiving treatment compared with those who did not had a greater number of DSM-IV diagnoses at baseline (P = .01), most strikingly, disruptive behavior disorders (58% vs 15%, P = .002). There was no association, however, between child treatment and maternal remission (P = .70), and the relation of maternal remission to child improvement was sustained after controlling for whether the child received any treatment during the 3-month follow-up interval (data available on request).

**COMMENT**

Many of the children of depressed mothers coming to STAR*D-Child were acutely symptomatic. Over a third had a current psychiatric disorder including anxiety (16%), depressive (10%), or disruptive behavior disorders (22%); almost half had a past psychiatric disorder. These high rates are consistent with findings from numerous studies of children of depressed parents.

The findings reported herein suggest that remission of maternal depression over 3 months is statistically sig-

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**Figure 3. Relation Between Maternal Response Level and Change in Child Diagnoses and Symptoms**

Diagnoses were based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Error bars represent 95% confidence intervals. Response levels reflect the percent reduction of maternal HAM-D between the baseline and 3-month evaluations.
nificantly associated with reduction in children’s current symptoms and diagnoses after controlling for the child’s age and sex, baseline symptoms, socioeconomic status (annual household income), as well as severity of maternal depression at baseline, mother’s treatment setting, and the child’s treatment status over the 3-month follow-up. Mothers in this study were treated with antidepressant medication, but it is likely that the findings reported herein would apply to any effective treatment of depression.

At least 50% maternal response to treatment was required to detect any reduction in child diagnoses and symptoms, and children of mothers who responded less than 50% showed an increase in diagnoses at 3 months. This finding is consistent with the 50% response threshold routinely used in the depression literature including the STAR*D adult study.31 There were no significant changes in children’s functioning at 3 months, but this lag is consistent with previous literature suggesting that a reduction in psychiatric symptoms often precedes improvement in functioning.38,39

Because our design was not experimental, we cannot demonstrate causality. Furthermore, children’s improvement may have had a positive impact on mothers (reverse causation). However, because the duration of the current maternal depressive episode at baseline was correlated with the number of children’s internalizing and externalizing symptoms at baseline (Cynthia Ewell-Foster, PhD, et al, unpublished data, December 2005), and the extent of children’s improvement following maternal remission depended on the magnitude of improvement in their mothers, reverse causation is not likely to fully account for the association between maternal remission and child improvement. It is more likely that maternal remission triggered improvement or prevented deterioration in the children and that this change in the children had further impact on the mothers. Thus, maternal remission seems to have initiated a virtuous cycle, wherein mothers and children positively influenced each other.

These findings need to be considered within the context of the remission rate, the low rate of women with children in the overall STAR*D study, and the study limitations. The remission rate at 3 months in this sample was 33%, and average time to remission was 55 days. If 50% response is considered, these rates increased to 47%. These rates are similar to those reported in the overall STAR*D study31 and are higher than those found in efficacy studies among patients with chronic depression.40 These remission rates should be viewed against the background of mothers participating in this study. They were moderately to severely depressed at baseline, with an average of 6 previous episodes and mean onset at age 20 years. Although more than a third of their children had a current psychiatric disorder at baseline and more than half had a lifetime history, some improvement was observed in the children in a relatively short time, ie, 3 months, and this occurred, in most cases, without the children receiving direct treatment. Even more interesting was the possible preventive impact of the intervention. Whereas children of unremitting mothers deteriorated (ie, acquired more symptoms and diagnoses) during the 3-month follow-up interval, none of the children of mothers whose depression had remitted had any onset or recurrence of a psychiatric disorder.

Only 22% of participating women who were aged 25 through 60 years had children aged 7 to 17 years. The low proportion of mothers among women seeking treatment suggests that depressed mothers compared with women without children might be less likely to seek and come for treatment. This finding is consistent with previous reports that depressed low-income women (a large proportion of the sample in this study) do not use community care available to them, even if it is free.40,41 Without outreach, child care, transportation, and flexible schedules, these women are not likely to receive appropriate treatment for their depression.

Child assessors knew that participating mothers were depressed. Thus, they were not blind to their initial diagnosis. However, assessors of child outcomes in the present study were unaware of maternal responses to treatment, and they were not involved in the mother’s treatment. As mentioned above, we cannot rule out the possibility that reverse causation (ie, changes in children’s psychopathology leading to reductions in maternal depressive symptoms) contributed to the association between maternal depression and child remission. It also is possible that some third variable not examined in the present study contributed to clinical changes in both the mother and the child (eg, change in levels of stress, financial strain). Although analyses were adjusted for the presence of a father in the household, we were unable to account for the impact of the fathers’ psychiatric state on their children because fathers were not directly assessed in the study.

Finally, maternal bias in reporting children’s symptoms may have influenced the CBCL data, which were based solely on maternal reports. Three points are worth noting with regard to CBCL scores. First, the duration of the current maternal depressive episode, but not the severity of this episode, was associated with the CBCL scores at baseline. Were depression-related bias to influence these scores, one would expect an association between maternal de-
pression severity and maternal reports. Second, findings obtained using CBCL scores were similar to those obtained using the Kiddie Schedule for Disorders and Schizophrenia, which are unlikely to be biased by maternal perception, as separate examinations of Kiddie Schedule for Disorders and Schizophrenia symptoms reported by mother and child revealed similar rates of depressive and anxiety symptoms. Finally, the lack of functional improvement in the children on the clinician-determined C-GAS were mirrored by a similar lack of improvement reported by the mother on the functional domains of the CBCL.

To our knowledge, this is the first published study to document prospectively the relation between remission of a mother's depression and her child's clinical state. These findings are intriguing because they suggest that an environmental influence (ie, the impact of maternal depression remission) had a measurable impact on the child's psychopathology. Recent studies show that the environmental may increase the onset of depressive disorders in genetically vulnerable adults and children. Our studies suggest that a reduction in stress associated with maternal remission may reverse the long-standing symptoms in children who are likely to be genetically vulnerable, although we have not genotyped the children in the study.

From a clinical vantage point, our findings suggest that vigorous treatment of depressed mothers to achieve remission is associated with positive outcomes in their children as well, whereas failure to treat depressed mothers may increase the burden of illness in their children. At a time when there are many questions about the appropriate and safe treatment of psychiatric disorders in children, these findings suggest that it is important to provide vigorous treatment to mothers if they are depressed.

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REFERENCES

lieve that it is essential for all clinical researchers to provide a complete disclosure of all financial interests that are relevant to a study. Although the term conflict of interest is widely used, it may entail different meanings. Margolis distinguishes between conflicting interests and conflicts of interest. The former occur in any situation for which competing considerations are presumed to be legitimate. Conflicts of interest, on the other hand, are characterized by an individual occupying dual roles, such as being a researcher and holding a significant financial interest in an area related to the research one is involved in.

At the time of submission of our manuscript to JAMA, we all reached an individual determination of whether our financial interests, which we report elsewhere, did or did not pose a relevant potential conflict of interest with this report. Our individual decisions were based on the recognition that the Sequenced Treatment Alternatives to Relieve Depression (STAR*D)—Child study was not designed or powered to demonstrate the efficacy of one antidepressant agent over others or of pharmacological strategies compared with either nonpharmacological treatments (including psychotherapy) or favorable environmental and temporal factors not related to clinical care. This point is made in the article, which provides important observations about mothers’ depressive remission and child health but which appropriately refrains from going beyond the data to test a particular agent or modality of treatment.

However, we recognize that JAMA policy requires disclosure of any potential conflicts of interest, and in retrospect we regret that we did not disclose all of our financial interests over the last 5 years and for the foreseeable future. They are included herein.

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