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Supplemental Methods

Interviewer Training and Quality Assurance

After the initial 2-day training, each interviewer observed three live interviews before conducting a supervised interview. Following completion of training, at least one directly observed interview and an acceptable reliability with the supervisor were required. Reliabilities between the interviewers and either of the child psychiatrists during the course of the study were obtained by comparing interviewers' ratings of a child from audiotape, scored by the child psychiatrist. The mean kappa for agreement on symptoms was 0.64 (range 0.54 to 0.81) and for diagnoses was 0.92 (range 0.60 to 1.00). Quality assurance activities included review of children's diagnostic assessments, monthly conference calls, site visits to ascertain compliance, and record reviews to insure completion and check for logical inconsistencies.

Items Used for the Negative Affectivity Score¹

GUILT	HOSTILITY/IRRITABILITY	FEAR/ANXIETY
HAM-D 2. Feeling of guilt MADRS 9. Pessimistic thoughts (guilt, inferiority, self-reproach, sinfulness, remorse, and ruin) QIDS-SR 11. (Negative) view of myself	SAS 5. Did you have any open argument with your friends in the last 2 weeks? SAS 11. Did you have any open argument with your relatives in the last 2 weeks? SAS 15. How often have you wanted to do the opposite of what your relatives wanted in order to make them angry during the last 2 weeks? SAS 24. Have you had any arguments with people at work in the last 2 weeks? SAS 31. Have you had any arguments with people (salespeople/tradesmen/neighbors) in the last 2 weeks? SAS 38. Have you had any arguments with your partner in the last 2 weeks? SAS 50. How have you been getting along with your children during the last 2 weeks? (Include only children over the age of 2 years)	HAM-D 10. Anxiety psychic SAS 16. How often have you been worried about things happening to your relatives without good reason in the last 2 weeks? SAS 25. Have you felt upset worried, or uncomfortable while doing your work during the last 2 weeks? SAS 53. How often have you been worried about your partner or any of your children without good reason in the last 2 weeks? MADRS 3. Inner tension QIDS 16. Feeling restless

Reference

1. Gerra ML, Marchesi C, Amat JA, et al: Does negative affectivity predict differential response to an SSRI versus a non-SSRI antidepressant? J Clin Psychiatry 2014; 75:e939–e944

TABLE S1. Sociodemographic and Clinical Characteristics of Depressed Mothers and Children by Maternal Treatment

Characteristic	Total (n = 76)	Treatment			Statistic ^a
		Combination (n = 27)	Bupropion (n = 20)	Escitalopram (n = 29)	
Mother					
Age, M (SD)	40.6 (6.4)	43.7 (6.4)	39.9 (5.6)	38.2 (5.7)	6.16**
Education, n (%)					
Some High School or Less	15 (19.7)	6 (22.2)	2 (10)	7 (24.1)	7.2
High School Graduate	18 (23.7)	6 (22.2)	5 (25)	7 (24.1)	
Some College	19 (25)	3 (11.1)	7 (35)	9 (31)	
College Graduate +	24 (31.6)	12 (44.4)	6 (30)	6 (20.7)	
Ethnicity, n (%)					
White	37 (48.7)	13 (48.1)	11 (55)	13 (44.8)	2.38
Black	2 (2.6)	1 (3.7)	1 (5)	0 (0)	
Hispanic	34 (44.7)	12 (44.4)	7 (35)	15 (51.7)	
Other ^b	3 (3.9)	1 (3.7)	1 (5)	1 (3.4)	
Marital status, n (%)					
Married with Spouse	33 (43.4)	14 (51.9)	4 (20)	15 (51.7)	6.06*
Single/Divorced/Separated	43 (56.6)	13 (48.1)	16 (80)	14 (48.3)	
Employment Status, n (%)					
Employed Full-time/Part-time	42 (55.3)	13 (48.1)	10 (50)	19 (65.5)	2.5
Homemaker	3 (3.9)	1 (3.7)	1 (5)	1 (3.4)	
Fulltime Student/Unemployed	23 (30.3)	10 (37)	6 (30)	7 (24.1)	
Other	8 (10.5)	3 (11.1)	3 (15)	2 (6.9)	
Receiving Public Assistance, n (%)	28 (36.8)	9 (33.3)	7 (35)	12 (41.4)	0.33
Household Income, n (%)					
Under \$15K	26 (34.2)	10 (37)	5 (25)	11 (37.9)	4.48
\$15-39K	12 (15.8)	3 (11.1)	6 (30)	3 (10.3)	
Over \$40K	35 (46.1)	14 (51.9)	8 (40)	13 (44.8)	
Children Per Family, M (SD)	1.8 (0.9)	2.0 (1.2)	1.8 (0.9)	1.6 (0.7)	1.36
Clinical Characteristics					
HAMD ₁₇ , M (SD)	21.8 (4.4)	23.3 (4.4)	21.8 (4.5)	20.4 (4.1)	2.99
MDD Severity (current), n (%) ^c					
Mild	4 (5.3)	1 (3.7)	1 (5)	2 (6.9)	6.41
Moderate	26 (34.2)	5 (18.5)	7 (35)	14 (48.3)	
Severe	46 (60.5)	21 (77.8)	12 (60)	13 (44.8)	
Any Anxiety Disorder, n (%)	27 (35.5)	8 (29.6)	7 (35)	12 (41.4)	0.85
Child					
Age, M (SD)	11.8 (3.3)	11.9 (3.4)	12.3 (3.3)	11.5 (3.3)	0.62
Living Status, n (%)					
Two Parent Household ^d	77 (57)	29 (53.7)	15 (42.9)	33 (71.7)	7.17*
Mother Only	58 (43)	25 (46.3)	20 (57.1)	13 (28.3)	
Female, n (%)	62 (45.9)	27 (50)	7 (20)	28 (60.9)	13.97**
Children Education, n (%)					
Grade 1-6	64 (47.4)	25 (46.3)	14 (40)	25 (54.3)	1.69
Above 6th Grade	71 (52.6)	29 (53.7)	21 (60)	21 (45.7)	
Any lifetime diagnosis, n (%)	65 (48.1)	29 (53.7)	17 (48.6)	19 (41.3)	1.53
Any current diagnosis, n (%)	58 (43)	23 (42.6)	16 (45.7)	19 (41.3)	0.16
Ever received any treatment, n (%)	34 (25.2)	16 (29.6)	11 (31.4)	7 (15.2)	3.9
Children's Depression Inventory, M (SD)	8.82(6.14)	7.2(5.5)	8.6(6.4)	10.5(5.9)	2.93
Columbia Impairment Scale, M (SD)	11.27(7.16)	10.2(7.1)	10.6(6.4)	12.6(8.2)	1.76

* p<0.05, ** p<0.01

Note. Numbers vary due to missing data. HAMD17 = Hamilton Rating Scale for Depression, 17-item; MDD = Major Depressive Disorder.

^at statistic for age comparisons, and chi-square statistic or Fisher's exact test for all other comparisons.

^bIncludes 1 American Indian, 1 parent who identified as more than 1 race, and 1 unknown.

^cSeverity defined as: mild, HAMD17<14; moderate, 14≤HAMD17≤21; severe, HAMD17≥22.

^dIncludes any combination of biological, adopted, or step mother and father.

TABLE S2. Relapse of Mothers from 0-12 Weeks by Treatment

Treatment	Mothers (n)	Children (n)	Relapsed at:
Combination ^a	3	7	4, 8, 12 wks
Bupropion ^b	1	3	8 wks
Escitalopram ^c	3	5	6, 10 wks
Total	7	15	

Note: No relapsers dropped out of the study.

^a 1 mother with 2 children relapsed at 4 weeks, 1 mother with 2 children relapsed at 8 weeks, and 1 mother with 3 children relapsed at 12 weeks.

^b 1 mother with 3 children relapsed at 8 weeks.

^c 1 mother with 2 children relapsed at 6 weeks, and 2 mothers with a total of 3 children relapsed at 10 weeks.

TABLE S3. Dropouts from 0-12 Weeks by Maternal Treatment

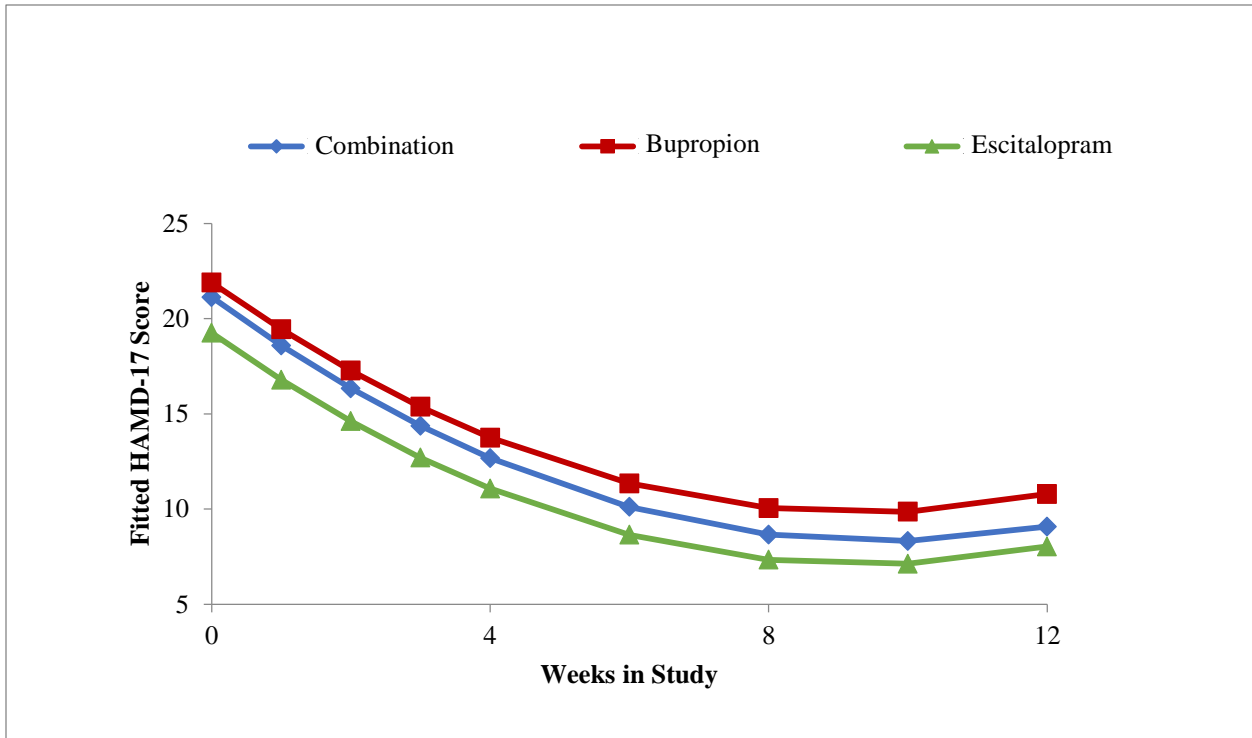
Treatment	Mothers (n)	Children (n)	Dropped out at:
Combination ^a	1	2	3 wks
Bupropion ^b	1	1	10 wks
Escitalopram ^c	2	2	2, 12 wks
Total	4	5	

^a 1 mother and her 2 children dropped out at 3 weeks.

^b 1 mother-child pair dropped out at 10 weeks.

^c 1 mother-child pair dropped out at 2 weeks, and 1 mother-child pair dropped out at 12 weeks.

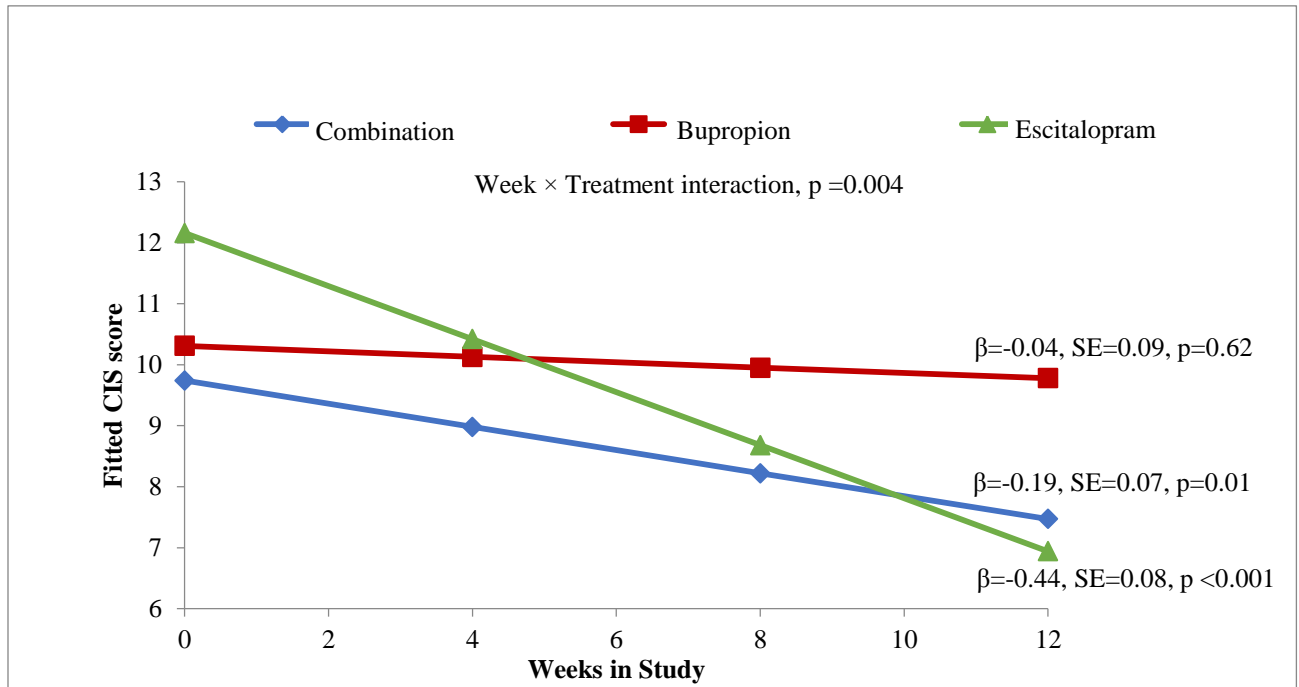
FIGURE S1. Estimated Trends in Mean HAMD-17 Scores Over 12 Weeks by Maternal Treatment Assignment



Note. Figure shows means of 27 combination-treated mothers, 20 bupropion-treated mothers, and 29 escitalopram-treated mothers. Lower scores indicate improvement. All analyses were adjusted for site.

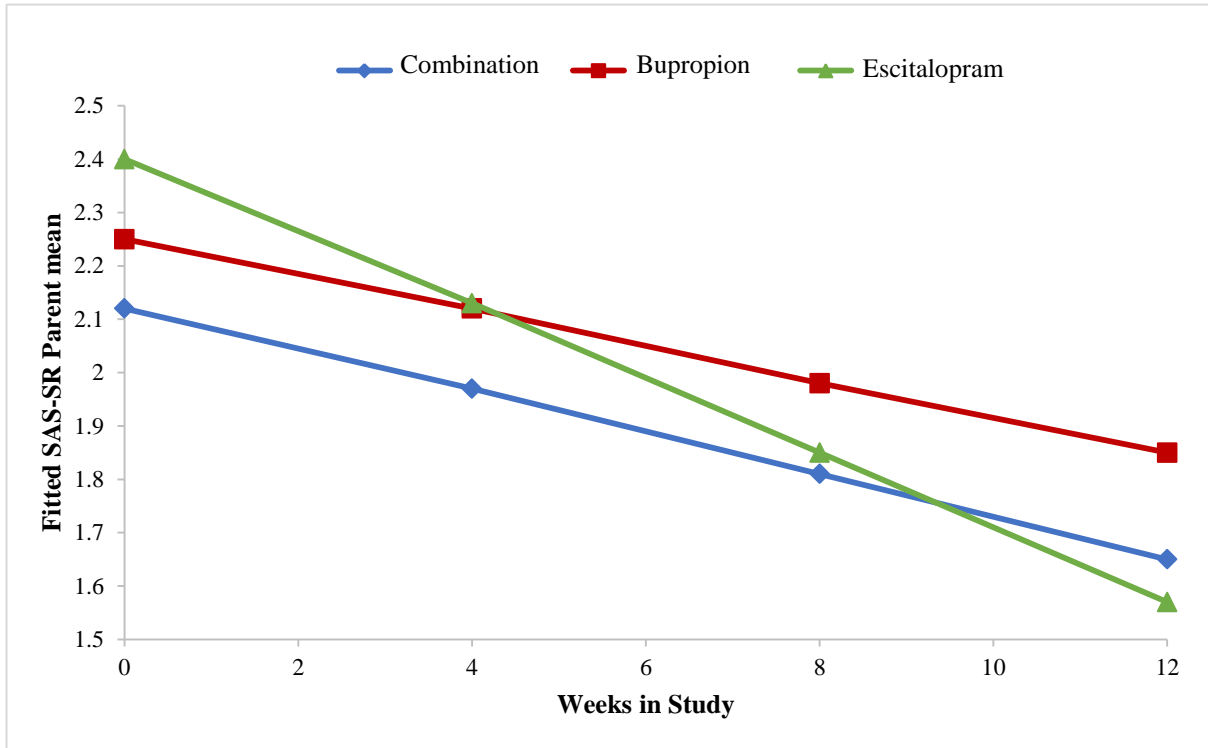
Overall, the negative linear component ($\text{Beta}_1 = -2.62$, $\text{SE} = 0.17$, $t = -15.22$, $p < 0.0001$) and positive quadratic component ($\text{Beta}_2 = 0.14$, $\text{SE} = 0.01$, $t = 9.85$, $p < 0.0001$) suggest that maternal HAMD-17 scores decreased significantly and then leveled off for all treatments over the 12-week study period. When factoring in both linear and quadratic components, the individual betas over time by treatment imply that mothers on combination treatment improved the most ($\text{Beta}_1 = -2.67$, $\text{SE} = 0.18$, $t = -14.59$, $p < 0.0001$; $\text{Beta}_2 = 0.14$, $\text{SE} = 0.01$, $t = 9.86$, $p < 0.0001$), followed by mothers on escitalopram ($\text{Beta}_1 = -2.60$, $\text{SE} = 0.18$, $t = -14.31$, $p < 0.0001$; $\text{Beta}_2 = 0.14$, $\text{SE} = 0.01$, $t = 9.86$, $p < 0.0001$) and mothers on bupropion ($\text{Beta}_1 = -2.60$, $\text{SE} = 0.19$, $t = -13.74$, $p < 0.0001$; $\text{Beta}_2 = 0.14$, $\text{SE} = 0.01$, $t = 9.86$, $p < 0.0001$). However, the overall week \times treatment interaction was not significant ($F = 0.30$, $df = 2, 539$, $p = 0.74$), meaning the change in HAMD-17 over time did not differ between treatment groups.

FIGURE S2. Estimated Trends in Mean CIS Scores Over 12 Weeks by Maternal Treatment Assignment



Note. CIS = Columbia Impairment Scale. Figure shows means of 54 children of 27 combination-treated mothers, 35 children of 20 bupropion-treated mothers, and 46 children of 29 escitalopram-treated mothers. Lower scores indicate improvement. All analyses were adjusted for child age (centered) and gender, site, and within-family correlation.

FIGURE S3. Estimated Trends in Mother’s Parental Functioning (SAS-SR) Score Over 12 Weeks by Maternal Treatment Assignment



Note. Figure shows means of 27 mothers receiving combination treatment, 20 mothers receiving bupropion, and 29 mothers receiving escitalopram. Lower scores indicate improvement. All analyses were adjusted for site. Time trends by treatment showed that mothers on escitalopram improved the most (Beta=-0.07, SE=0.01, t=-5.73, p<0.0001), followed by those on combination (Beta=-0.04, SE=0.01, t=-3.67, p=0.0003) and bupropion treatment (Beta=-0.03, SE=0.01, t=-2.64, p=0.009). The overall week × treatment interaction reached trend-level significance (F=2.48, df=2,152, p=0.09), meaning there is a suggestion that the change in SAS-SR parent subscale score over time may differ between treatment groups. Pairwise comparisons showed significant differences between mothers on bupropion vs. escitalopram (Beta=0.04, SE=0.02, t=2.02, p=0.04), trend-level differences between mothers on combination vs. escitalopram (Beta=0.03, SE=0.01, t=1.84, p=0.07), and no significant differences between mothers on combination vs. bupropion (Beta=-0.01, SE=0.02, t=-0.35, p=0.73).

TABLE S4. Effect of Maternal Treatment Assignment on Trends in Maternal Social-Parental Functioning Over 12 Weeks

Outcome ^a	Baseline	Beta	SE	p	Change over time
Total SAS-SR overall functioning					
Combination treatment	2.1	-0.061	0.008	<.0001	-0.732
Bupropion	2.2	-0.038	0.010	<.0001	-0.456
Escitalopram	2.3	-0.048	0.008	<.0001	-0.576
Group-by-time		F=1.7		0.18	
Combination vs bupropion (ref)		-0.023	0.013	0.07	
Combination vs escitalopram (ref)		-0.013	0.012	0.26	
Bupropion vs escitalopram (ref)		0.010	0.013	0.43	
SAS-SR Parental functioning^b					
Combination treatment	2.1	-0.039	0.011	0.0003	-0.468
Bupropion	2.2	-0.034	0.013	0.009	-0.408
Escitalopram	2.3	-0.069	0.012	<0.0001	-0.828
Group-by-time		F=2.48		0.09	
Combination vs bupropion (ref)		-0.006	0.017	0.73	
Combination vs escitalopram (ref)		0.030	0.016	0.07	
Bupropion vs escitalopram (ref)		0.035	0.018	0.04	
SAS-SR Parenting Item 1					
Combination treatment	2.1	-0.037	0.017	0.03	-0.444
Bupropion	2.2	-0.043	0.020	0.03	-0.516
Escitalopram	2.3	-0.061	0.019	0.002	-0.732
Group-by-time		F=0.47		0.62	
Combination vs bupropion (ref)		0.006	0.026	0.82	
Combination vs escitalopram (ref)		0.024	0.025	0.34	
Bupropion vs escitalopram (ref)		0.018	0.018	0.51	
SAS-SR Parenting Item 2					
Combination treatment	2.0	-0.034	0.015	0.02	-0.408
Bupropion	2.4	-0.051	0.017	0.004	-0.612
Escitalopram	2.6	-0.097	0.017	<0.0001	-1.164
Group-by-time		F=4.12		0.02	
Combination vs bupropion (ref)		0.017	0.023	0.47	
Combination vs escitalopram (ref)		0.063	0.022	0.005	
Bupropion vs escitalopram (ref)		0.046	0.024	0.057	
SAS-SR Parenting Item 3					
Combination	2.0	-0.049	0.017	0.005	-0.588
Bupropion	2.4	-0.033	0.020	0.11	-0.396
Escitalopram	2.6	-0.056	0.020	0.005	-0.672
Group-by-time		F=0.36		0.70	
Combination vs bupropion (ref)		-0.017	0.027	0.53	
Combination vs escitalopram (ref)		0.006	0.026	0.81	
Bupropion vs escitalopram (ref)		0.023	0.028	0.41	
SAS-SR Parenting Item 4					
Combination	2.0	-0.044	0.013	0.0005	-0.528
Bupropion	2.4	-0.013	0.015	0.39	-0.156
Escitalopram	2.6	-0.045	0.014	0.001	-0.540
Group-by-time		F=1.72		0.18	
Combination vs bupropion (ref)		-0.032	0.019	0.10	
Combination vs escitalopram (ref)		0.001	0.019	0.97	
Bupropion vs escitalopram (ref)		0.032	0.020	0.11	

Note. Total N = 76 mothers: 27 on combination treatment, 20 on bupropion, and 29 on escitalopram. All analyses were adjusted for site.

^aA decrease over time indicates improvement for all measures.

^bSAS-SR Parenting Items: (1) Been interested in your children's activities, e.g. school/friends/etc.? (2) Been able to talk to and listen to your children? (3) Been shouting at or arguing with your children? (4) Been feeling affectionate towards your children?

TABLE S5. Effect of Maternal Treatment Assignment on Child's Report of the Mother's Affection and Care (PBI) Over 12 Weeks

Outcome ^a	Baseline	Beta	SE	p	Change over time
Parental Bonding Inventory^b					
Combination treatment	30.0	-0.089	0.089	0.30	-1.068
Bupropion treatment	28.1	-0.089	0.094	0.34	-1.068
Escitalopram treatment	26.6	0.167	0.084	0.047	2.004
Group-by-time		F=2.99		0.053	
Combination vs bupropion (ref)		-0.001	0.127	> 0.99	
Combination vs escitalopram (ref)		-0.257	0.120	0.03	
Bupropion vs escitalopram (ref)		-0.256	0.126	0.04	

Note. N= 54 children of 27 combination-treated mothers, 35 children of 20 bupropion-treated mothers, and 46 children of 29 escitalopram-treated mothers. The Care measure of the Parental Bonding Inventory (PBI) child report on mother (COM) was adjusted for child age and gender, and for site. Due to having only two assessment points, it was not possible to adjust for within-family correlation.

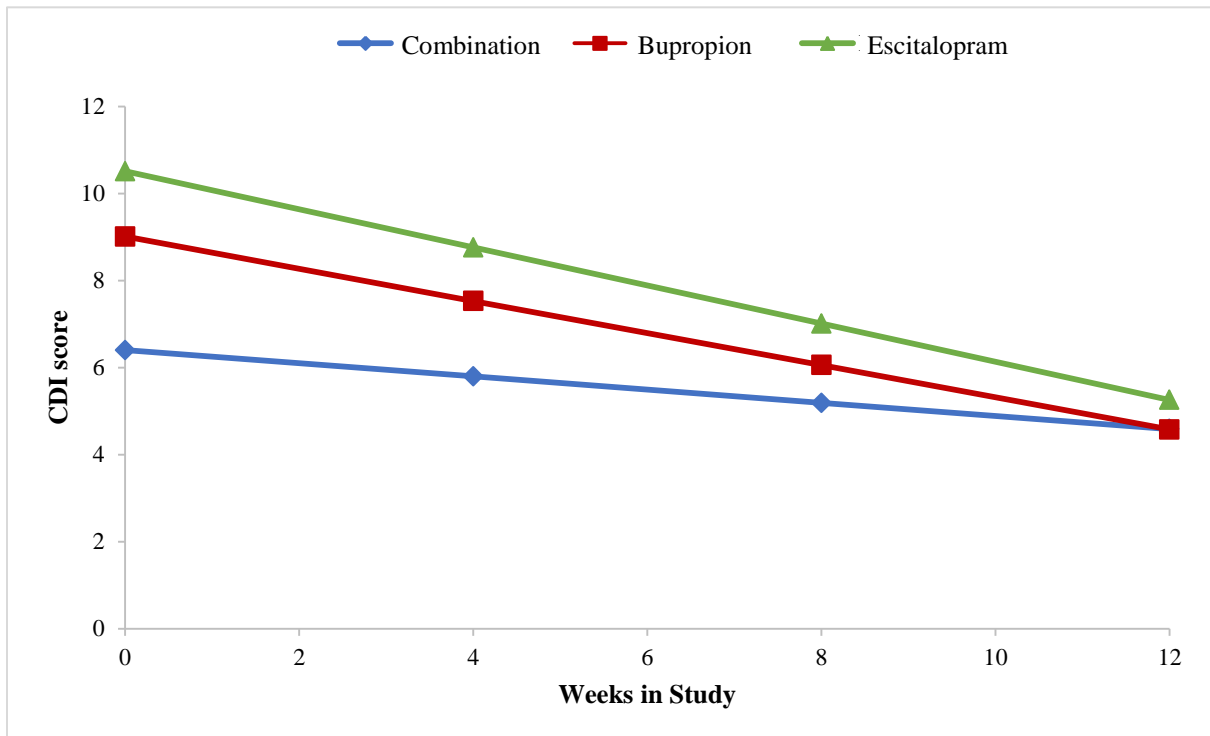
^aAn increase over time indicates improvement for PBI-COM Care.

^bPBI Child On Mother (COM) interpretation: The individual betas over time by treatment imply that children of escitalopram-treated mothers (Beta=0.17, SE=0.08 t=2.00, p=0.047) improved significantly, while those of both combination- (Beta=-0.09, SE=0.09, t=-1.04, p=0.30) and bupropion-treated (Beta=-0.09, SE=0.09, t=-0.95, p=0.35) mothers worsened. The overall week × treatment interaction reached marginal significance (F=2.99, df= 2,164, p=0.053), suggesting that the change in child-reported score of the mother's care over time may differ between treatment groups. Pairwise comparisons showed significant differences between children of mothers receiving combination vs escitalopram treatment (Beta=-0.26, SE=0.12, t=-2.14, p=0.03) and between bupropion and escitalopram (Beta=-0.26, SE=0.13, t=-2.04, p=0.04), while there were no significant differences between combination and bupropion (Beta=-0.001, SE=0.13, t=-0.01, p>0.99).

PBI Care and Affection items

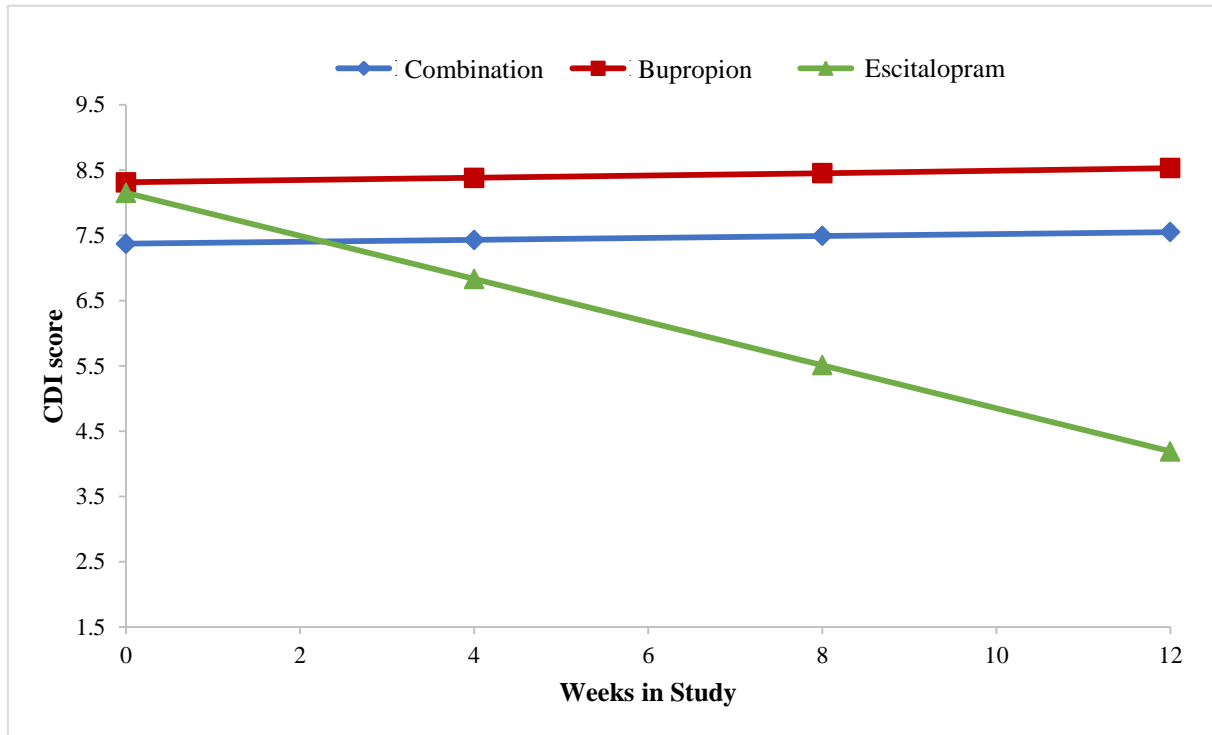
1. Spoke to me with a warm and friendly voice
2. Did not help me as much as I needed
4. Seemed emotionally cold to me
5. Appeared to understand my problems and worries
6. Was affectionate to me
11. Enjoyed talking things over with me
12. Frequently smiled at me
14. Did not seem to understand what I needed or wanted
16. Made me feel I wasn't wanted
17. Could make me feel better when I was upset
18. Did not talk with me very much
24. Did not praise me

FIGURE S4. Depressive Symptoms in Children by Mothers' Treatment in Mothers with Baseline Low Negative Affectivity



Note. Higher scores on the Children's Depression Inventory (CDI) indicate greater levels of depression. The overall week \times treatment interaction was not significant ($F=2.81$, $df=2,114$, $p=0.064$), suggesting that CDI changes over time did not differ between treatment groups, in mothers with low negative affectivity at baseline. Individual betas showed that children of mothers treated with escitalopram ($Beta=-0.43$, $SE=0.08$, $p<0.0001$), combination treatment ($Beta=-0.15$, $SE=0.07$, $p=0.04$), and bupropion ($Beta=-0.36$, $SE=0.11$, $p=0.005$) changed significantly over time.

FIGURE S5. Time Trends in Depressive Symptoms in Children by Mothers' Treatment in Mothers with Baseline High Negative Affectivity



Note. Higher scores on the Children's Depression Inventory (CDI) indicate greater levels of depression. The overall week \times treatment interaction was significant ($F=4.84$, $df=2,113$, $p<0.01$), suggesting that CDI changes over time differed between treatment groups, in mothers with high negative affectivity at baseline. Individual betas showed that only children of mothers treated with escitalopram ($Beta=-0.33$, $SE=0.09$, $p=0.001$) showed a significant reduction on the CDI. Children of mothers with high negative affectivity at baseline who received combination treatment ($Beta=0.03$, $SE=0.09$, $p=0.77$) and bupropion ($Beta=0.02$, $SE=0.10$, $p=0.85$) showed a non-significant change over time.

TABLE S6. Distribution of Baseline Negative Affectivity (Low/High) by Treatments

Negative Affectivity	Treatment			Chi-Square	p
	Combination (n=27)	Bupropion (n=20)	Escitalopram (n=29)		
Low	9 (33.3%)	12 (60.0%)	17 (58.6%)	4.66	0.10
High	18 (66.7%)	8 (40.0%)	12 (41.4%)		