

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. MONEAD Clinical Sites and Investigators

MONEAD Clinical Sites

Augusta University
Columbia University
Emory University
Geisinger Clinic
Harvard University (Brigham & Women's Hospital)
Henry Ford Hospital (Wayne State University)
Johns Hopkins University
Minnesota Epilepsy Group
New York University
Northwell Health
Northwestern University
Stanford University
University of Alabama at Birmingham
University of Arizona
University of Cincinnati
University of Miami
University of Pittsburgh
University of Southern California
University of Washington
Wake Forest University Health Sciences

MONEAD Investigator Group

Executive Committee: Kimford J. Meador, MD (Stanford University, Multiple PI and Executive Committee Director); Page B. Pennell, MD (Harvard University, Brigham & Women's Hospital, Multiple PI and Co-Director of Semiology Core); Ryan May, PhD (previously with The Emmes Company, former Multiple PI and Director of Data & Statistical Center); Abigail G. Matthews, PhD (The Emmes Company, Multiple PI and Director of Data & Statistical Center); Angela Birnbaum, PhD (University of Minnesota, Director of Pharmacokinetics Core); Morris J. Cohen, EdD (Pediatric Neuropsychology International, Co-Director of Neuropsychology Core); Maurice Druzin, MD (Stanford University, Co-Director of OB Core); Richard Finnell, PhD (Baylor College of Medicine, Consultant on Teratogenicity); Jacqueline French, MD (New York University, Co-Director, Semiology Core); Gregory Holmes, MD (University of Vermont, Consultant); David W. Loring, PhD (Emory University, Co-Director, Neuropsychology Core and Chair, Publications Committee); Frederick T. McElrath, MD (Harvard University, Brigham & Women's, Co-Director of OB Core); Lorene Nelson, PhD (Stanford University, Consultant); Zachary Stowe, MD (University of Wisconsin, Director of Psychiatric Core); Linda Van Marter, MD (Harvard University, Brigham & Women's, Director of Neonatal Core); Peter Wells, PharmD (University of Toronto, Consultant); Mark Yerby, MD (Oregon Health Sciences University, Consultant); Eugene Moore, BS (Emory University, Multisite Research Project Manager).

Data & Statistical Center: (The Emmes Company): Abigail G. Matthews, PhD (Multiple PI and Director of Data & Statistical Center); Dominic Ippolito, MS (Project Manager), Carrie Brown, MS (Statistician), Chelsea Robalino, MStat (Statistician), Lisa Davis, BA (Administrative Coordinator), Nilay Shah, MD (Medical Monitor), Brenda Leung, BS (Programmer Analyst), Mark Friedman, MS (Clinical Systems Analyst), Traci Sheer, BA (Data Manager/Protocol Monitor), Yue Wang, MS (SAS Programmer).

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Augusta University: Suzanne Strickland, MD (site PI); Erin Latif, MD (OB Co-Investigator); Yong Park, MD (OB Co-Investigator); Delmaris Acosta-Cotte, MA (Site Neuropsychologist); Patty Ray, PhD (research assistant);

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University of Arizona: David Labiner, MD (site PI); James Maciulla, MD (OB Co-Investigator); Jennifer Moon, PsyD (Site Neuropsychologist); Kayla Darris, BA (research assistant);

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Multisite: Danielle Miller, MA (Project Traveling Neuropsychologist).

eAppendix 2. Additional Details of Outcomes

Expressive Language Index (ELI) was calculated as the average of the following two assessments:

- Scaled Naming Vocabulary subtest from DAS-2¹ (re-scaled to have Mean = 100 and Standard Deviation = 15)
- Expressive Communication subscale from PLS-5²

If missing score for any subscale, then ELI was set to missing.

Receptive Language Index (RLI) was calculated as the average of the following three assessments:

- Scaled Verbal Comprehension subtest from DAS-2¹ (re-scaled to have Mean = 100 and Standard Deviation = 15)
- Auditory Comprehension subscale from PLS-5²
- PPVT-4³ Score

If missing score for any subscale, then RLI was set to missing.

DAS-2 = Differential Abilities Scale, Second Edition

PLS-5 = Preschool Language Scale, Fifth Edition

PPVT-4 = Peabody Picture Vocabulary Test, Fourth Edition

1. Elliott CD. Differential Ability Scales (2nd edition). San Antonio, TX: Harcourt Assessment, 2007.
2. Zimmerman, IL, Steiner, VG, Pond, RE. Preschool Language Scale, Fifth Edition. Bloomington, MN: Pearson Education, Inc/PsychCorp, 2011.
3. Dunn L, Dunn D. Peabody Picture Vocabulary Test. 4th ed. Minneapolis, MN: Pearson Assessments, 2007.

eAppendix 3. Additional Details of Statistical Analyses

Primary Analysis Models:

Covariates for Primary Analysis #1: Mother's study group, IQ, education level, age at enrollment, illicit substance use during pregnancy, major depressive episode during pregnancy, post-birth perceived stress (PSS) score, and child's sex, birthweight, and small for gestational age.

Covariates for Primary Analysis #2: Mother's third trimester max observed ratio ASM Concentration, IQ, education level, age at enrollment, smoking during pregnancy, post-birth anxiety (BAI) score, ASM group (Monotherapy/Polytherapy), McMaster FAD problematic family functioning at child's 2-year visit, and child's sex, small for gestational age.

Mother's max ratio defined daily dose (DDD) during the third trimester was not considered for inclusion in the model for primary analysis 2 due to collinearity with ratio blood levels in the third trimester.

Calculation of Ratio of ASM Blood Concentration and Ratio of Defined Daily Dose

To compare exposure across ASMs combined, the ratio of ASM blood concentration and ratio of defined daily dose (ratio DDD) were derived as follows:

The ratio of ASM blood concentration was calculated for each ASM by dividing the maternal ASM concentration by the upper limit of the suggested therapeutic ranges, mostly taken from published ranges,¹ or clinical laboratory references used by Stanford clinics. For mothers on polytherapy at the time of blood draw, the sum of the ratio of ASM blood concentration across all ASMs was used for analysis and was computed only if all ASMs mothers were taking were measured. ASM concentrations below lower limit of quantification were included and imputed as ½ the lower level of quantification (LLoQ) for that ASM. ASM blood concentrations below lower limit of detection and collected less than 72 hours after the last dose were included and imputed with a concentration value of 0.001 for analysis. ASM blood concentrations below lower limit of detection from blood samples collected 72 hours or more after the mother's last dose were set to missing and the ratio of ASM concentration was not calculated. The maximum observed ratio ASM concentration within the 3rd trimester, including the ASM concentration from the day of delivery, was used for analysis.

ASM (ug/mL)	Lower Limit	Upper Limit	LLoQ
Carbamazepine	4	12	0.31
Gabapentin	4	20	0.06
Lacosamide	1	10	0.1
Lamotrigine	2.5	15	0.31
Levetiracetam	10	40	0.1
Oxcarbazepine	10	40	0.5
Phenobarbital	15	40	0.5
Phenytoin	10	20	0.5

Pregabalin	2	5	0.06
Topiramate	10	20	0.38
Valproate	50	100	-
Zonisamide	10	40	0.63

The ratio DDD was calculated by dividing the maternal ASM dose by the WHO defined daily dose values². The sum of the ratio DDDs across all ASMs were used for polytherapies. The maximum ratio DDD within the 3rd trimester was used for analyses with dose. Employing DDD provided a larger sample size than ASM concentrations.

ASM (mg/day)	DDD
Carbamazepine	1000
Clonazepam	8
Ethosuximide	1250
Felbamate	2400
Gabapentin	1800
Lacosamide	300
Lamotrigine	300
Levetiracetam	1500
Oxcarbazepine	1000
Phenobarbital	100
Phenytoin	300
Pregabalin	300
Topiramate	300
Valproate	1500
Zonisamide	200

ASM exposure analyses were restricted to children of women with epilepsy on ASM at enrollment.

1. St Louis EK. Minimizing AED adverse effects: improving quality of life in the interictal state in epilepsy care [published correction appears in *Curr Neuropharmacol*. 2010;8(1):82]. *Curr Neuropharmacol*. 2009;7(2):106-114.
2. WHO Collaborating Centre for Drug Statistics Methodology. WHO ATC/DDD Index 2021. https://www.whocc.no/atc_ddd_index/ (updated December 17, 2020. (accessed 4/9/2022).

Variables included in Imputation Models

Separate imputation models were used for analyses of children of women with epilepsy (WWE) and women without epilepsy (WWoE) and for analyses of children of WWE on ASM. The imputation model for children of WWE and WWoE included the following variables a priori: mother's study group, mother's IQ, all risk factors, and covariates selected using the stepwise selection algorithm. The imputation model for children of WWE with 3rd trimester ASM concentrations included the following variables a priori: maximum observed 3rd trimester ratio ASM concentration, mother's IQ, maximum 3rd

trimester ratio DDD, all risk factors, and covariates selected using the stepwise selection algorithm. Additional potential covariates and the indicator variable for twin birth (Y/N) were assessed for inclusion in the imputation models and were included if they met one of the following criteria. These criteria were assessed separately for each of the imputation models:

- Associated with age 4.5 ABAS-3 general adaptive composite (GAC) score in univariate analysis ($p < 0.2$)
- Associated with pattern of missingness in age 4.5 ABAS-3 GAC score ($p < 0.2$)

Since variables included in the imputation model must be linearly independent. If two or more linearly dependent variables were selected to be included in the imputation model based on the above criteria, the variable with the most categories was included in the model. Variables with >5% missing were excluded from consideration.

Variables included in imputation model for children of women with and without epilepsy:

mother's study group, IQ, age at enrollment, weeks gestational age at enrollment, weeks gestational age at delivery, mother's education level, breastfeeding, folate dose, employment status, household income, planned/welcome pregnancy, major depressive episode during pregnancy, smoking and illicit substance use during pregnancy, lifetime history of anxiety disorder, lifetime history of mood disorder, average anxiety score (BAI), depression score (BDI), and perceived stress score (PSS) during enrollment through 2-year post-birth, enrollment through delivery, and post-delivery through 2-year post-birth, McMaster FAD problematic family functioning at child's 2-year visit, child's sex, birthweight, and small for gestational age.

Variables included in imputation model for children of women with epilepsy on ASM in

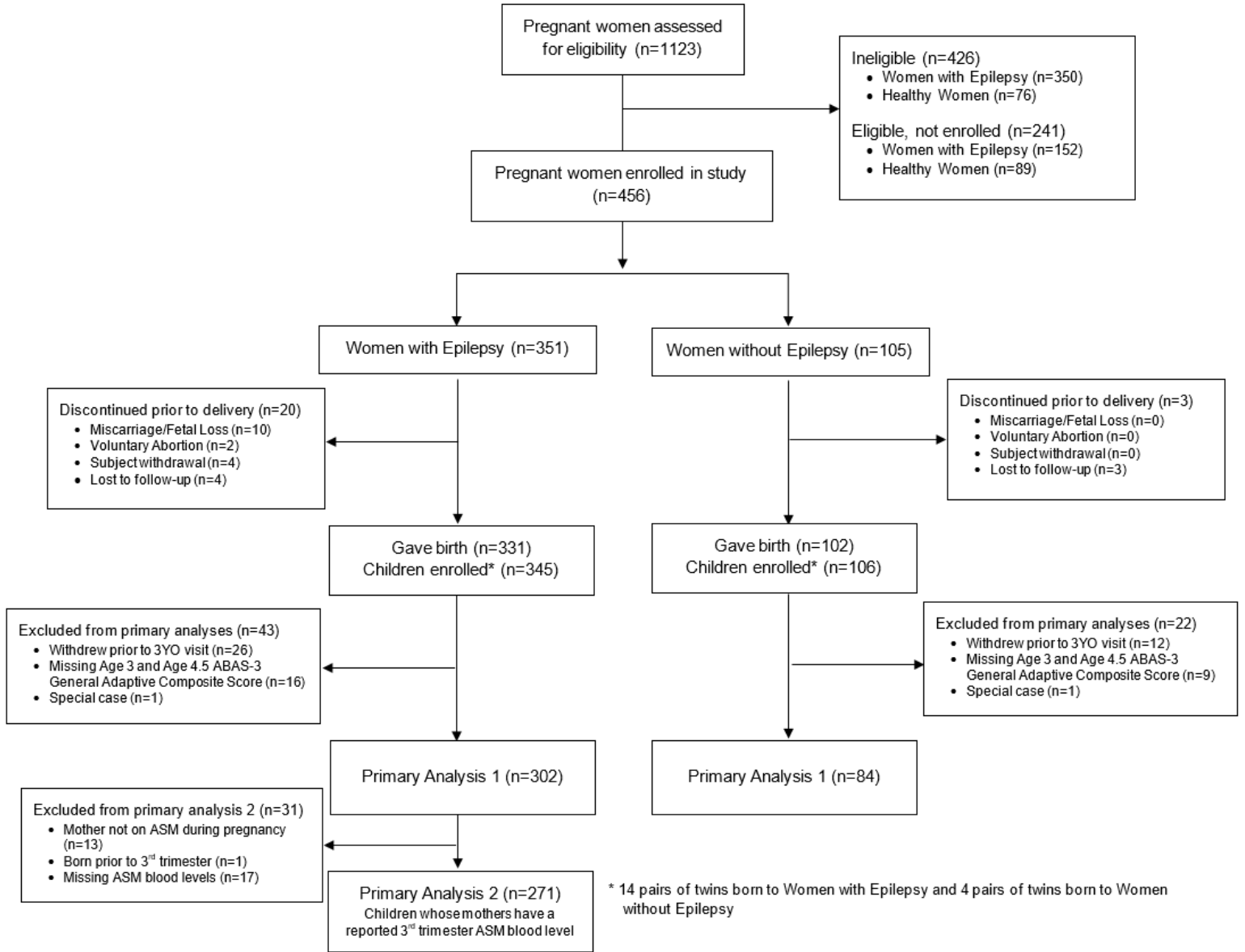
3rd trimester: mother's max observed ratio ASM concentration and ratio DDD in 3rd trimester, IQ, weeks gestational age at enrollment, weeks gestational age at delivery, mother's education level, household income, breastfeeding, folate dose, employment status, planned/welcome pregnancy, smoking and illicit substance use during pregnancy, lifetime history of anxiety disorder, lifetime history of mood disorder, ASM group, age at enrollment, average anxiety score (BAI), depression score (BDI), and perceived stress score (PSS) during enrollment through 2-year post-birth, enrollment through delivery, and post-delivery through 2-year post-birth, McMaster FAD problematic family functioning at child's 2-year visit, child's sex, birthweight, and small for gestational age.

Special Cases

Two special cases were excluded from all analyses.

- Child of woman with epilepsy with a donated ovum
- Child of woman without epilepsy on ASM during pregnancy

eFigure. Flowchart of Enrollment and Exclusions



eTable 1. Children With Non-Missing Assessments at Ages 2, 3, 4.5

Children with Non-Missing Assessments, N = 451	
Assessment	n (%)
Age 2	
Behavior Assessment System for Children, Second Edition (BASC-2)	386 (85.6)
Modified Checklist for Autism in Toddlers (MCHAT)	397 (88.0)
Parenting Stress Index, Fourth Edition (PSI-4)	388 (86.0)
Age 3	
Adaptive Behavior Assessment System, Third Edition (ABAS-3)	374 (82.9)
Behavior Assessment System for Children, Second Edition (BASC-2)	374 (82.9)
Gilliam Autism Rating Scale, Third Edition (GARS-3)	368 (81.6)
Parenting Stress Index, Fourth Edition (PSI-4)	367 (81.4)
Age 4.5	
Adaptive Behavior Assessment System, Third Edition (ABAS-3)	329 (72.9)
Behavior Assessment System for Children, Second Edition (BASC-2)	330 (73.2)
Parenting Stress Index, Fourth Edition (PSI-4)	328 (72.7)
Social Responsiveness Scale, Second Edition (SRS-2)	331 (73.4)

eTable 2. ABAS-3 General Adaptive Composite Scores at Age 4.5, Before vs After COVID-19 Shutdown, Completers Population, N = 326

	ABAS-3 General Adaptive Composite Scores at Age 4.5			
	N	Mean (95% CI)	Median (Min, Max)	P-Value^a
Before COVID-19 Shutdown	234	101.1 (99.5, 102.6)	101 (49, 120)	0.942
After COVID-19 Shutdown	92	101.2 (98.8, 103.5)	100 (52, 120)	

Notes: COVID-19 shutdown defined as April 1, 2020. There were no children evaluated between March 13, 2020 and June 30, 2020.

N = children with ABAS-3 general adaptive composite scores at age 4.5.

^a Independent T-test.

To assess the impact of the COVID-19 shutdown, the primary outcome for this manuscript, ABAS-3 General Adaptive Composite scores at age 4.5, were compared before vs. after April 1, 2020. An independent T-test was run, and no difference were found between scores before and after the COVID-19 shutdown. Thus, the impact of COVID-19 was not further considered in this manuscript.

eTable 3. Summary of Mother's 3rd Trimester ASM

	Primary Analysis 1 ^a N = 302	Primary Analysis 2 ^b N = 271
Mother's 3rd Trimester ASM Regimen	n (%)	n (%)
Monotherapy	226 (74.8)	219 (80.8)
Lamotrigine	99 (32.8)	98 (36.2)
Levetiracetam	78 (25.8)	77 (28.4)
Oxcarbazepine	16 (5.3)	14 (5.2)
Carbamazepine	11 (3.6)	10 (3.7)
Zonisamide	11 (3.6)	10 (3.7)
Topiramate	4 (1.3)	4 (1.5)
Lacosamide	2 (0.7)	2 (0.7)
Valproate	2 (0.7)	2 (0.7)
Felbamate	1 (0.3)	-
Gabapentin	1 (0.3)	1 (0.4)
Phenobarbital	1 (0.3)	1 (0.4)
Polytherapy	62 (20.5)	52 (19.2)
Lamotrigine+Levetiracetam	27 (8.9)	25 (9.2)
Lacosamide+Levetiracetam	5 (1.7)	5 (1.8)
Other Polytherapy ^c	30 (9.9)	22 (8.1)
No ASM in Pregnancy	13 (4.3)	-
No ASM in 3rd Trimester^d	1 (0.3)	-

^a N = children of WWE in primary analysis 1. Mother's ASM regimen at time of blood draw for maximum observed ratio ASM concentration during 3rd trimester (includes day of delivery) or if missing ASM concentration then ASM regimen for maximum ratio DDD during 3rd trimester.

^b N = children in primary analysis 2. Mother's ASM regimen at time of blood draw for maximum observed ratio ASM concentration during 3rd trimester (includes day of delivery).

^c Other polytherapy includes three or fewer children with mothers on Carbamazepine+Lamotrigine, Carbamazepine+Levetiracetam, Clonazepam+Lamotrigine, Ethosuximide+Lamotrigine, Ethosuximide+Lamotrigine+Levetiracetam+Zonisamide, Felbamate+Oxcarbazepine+Topiramate, Gabapentin+Lamotrigine, Lacosamide+Lamotrigine, Lacosamide+Topiramate, Lamotrigine+Levetiracetam+Zonisamide, Lamotrigine+Oxcarbazepine, Lamotrigine+Oxcarbazepine+Valproate, Lamotrigine+Pregabalin, Lamotrigine+Topiramate, Lamotrigine+Valproate, Lamotrigine+Zonisamide, Levetiracetam+Oxcarbazepine, Levetiracetam+Phenobarbital, Levetiracetam+Phenytoin, Levetiracetam+Topiramate, Levetiracetam+Zonisamide, Oxcarbazepine+Zonisamide.

^d One child was born in the second trimester and had no 3rd trimester ASM exposure. Mother was on Levetiracetam monotherapy during pregnancy.

eTable 4. Demographic, Baseline Characteristics, and Risk Factors for Children of WWE vs WWoE, Categorical Variables, Children in Primary Analysis 1, N = 386

	Children of WWE, N = 302	Children of WWoE, N = 84	
	n (%)	n (%)	P-Value ^a
Child's Sex			0.326
Female	159 (52.6)	39 (46.4)	
Male	143 (47.4)	45 (53.6)	
Child's Race			0.008
White	243 (80.5)	55 (65.5)	
Black or African American	15 (5.0)	11 (13.1)	
Other/Unknown	44 (14.6)	18 (21.4)	
Child's Ethnicity - Hispanic or Latino	57 (18.9)	20 (23.8)	0.354
Twin	23 (7.6)	6 (7.1)	1.000
Small for Gestational Age (SGA)	17 (5.8)	7 (8.4)	0.444
Missing	8	1	
Major Congenital Malformations	18 (6.0)	1 (1.2)	0.089
Any Breastfeeding	232 (77.1)	75 (89.3)	0.014
Missing	1	0	
Periconceptual Folate Use	268 (88.7)	56 (66.7)	<.001
Periconceptual Folate Dose			<.001
0 mg	34 (11.4)	28 (34.1)	
> 0 - 0.4 mg	25 (8.4)	13 (15.9)	
> 0.4 - 1 mg	58 (19.4)	32 (39.0)	
> 1 - 4 mg	160 (53.5)	9 (11.0)	
> 4 mg	22 (7.4)	0 (0.0)	
Missing	3	2	
Pregnancy Planned/Welcomed			0.499
Planned	220 (72.8)	56 (66.7)	
Unplanned/Welcome	73 (24.2)	25 (29.8)	
Unplanned/Unwelcome	9 (3.0)	3 (3.6)	
Major Depressive Episode During Pregnancy^b	12 (4.0)	1 (1.2)	0.314
Mother's Education			0.284
College Degree (Advanced)	82 (27.2)	30 (35.7)	
College Degree (Not Advanced)	137 (45.4)	32 (38.1)	
No College Degree	83 (27.5)	22 (26.2)	
Mother's Employment			0.456
Employed full-time	169 (56.0)	46 (54.8)	

	Children of WWE, N = 302	Children of WWoE, N = 84	
	n (%)	n (%)	P-Value ^a
Employed part-time	45 (14.9)	17 (20.2)	
Unemployed ^c	88 (29.1)	21 (25.0)	
Household Income			0.918
Subject desires not to answer	17 (5.6)	4 (4.8)	
\$24,999 or less	50 (16.6)	15 (17.9)	
\$25,000-49,999	33 (10.9)	7 (8.3)	
\$50,000-74,999	43 (14.2)	9 (10.7)	
\$75,000-99,999	53 (17.5)	17 (20.2)	
\$100,000 and up	106 (35.1)	32 (38.1)	
Smoking^d	19 (6.3)	5 (6.0)	1.000
Alcohol Use^d	70 (23.2)	32 (38.1)	0.008
Illicit Substance Use^d	9 (3.0)	4 (4.8)	0.490
Missing	1	1	
McMaster FAD Problematic Family Functioning at Child's 2YO Visit	53 (18.5)	12 (14.6)	0.512
Missing	16	2	
Lifetime History of Mood Disorder^e	49 (16.5)	11 (13.6)	0.609
Missing	5	3	
Lifetime History of Anxiety Disorder^e	47 (15.8)	12 (14.8)	1.000
Missing	5	3	

FAD = Family Assessment Device

Note: Missing not used in calculation of percentages or in p-values.

^a P-Values from Fisher's Exact Test.

^b Depression based on SCID Mood Module at any depression assessment during pregnancy.

^c Unemployed includes stay at home parent without outside job, unemployed due to disability, full-time student and looking for work.

^d Self-reported smoking, alcohol use, or illicit substance use (including marijuana) at any time during pregnancy.

^e Diagnosis from SCID.

eTable 5. Demographic, Baseline Characteristics, and Risk Factors for Children of WWE vs WWoE, Continuous Variables, Children in Primary Analysis 1, N = 386

	Children of WWE, N = 302			Children of WWoE, N = 84			P-Value ^a
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)	
WGA at Birth	302	38.4 (38.2, 38.7)	39 (24, 42)	84	38.6 (38.1, 39.0)	39 (26, 43)	0.651
WGA at Enrollment	302	13.5 (12.9, 14.0)	14 (4, 29)	84	15.5 (14.6, 16.3)	16 (5, 23)	<.001
Birthweight (kg)	295	3.22 (3.16, 3.29)	3.2 (0.6, 4.9)	84	3.26 (3.13, 3.39)	3.3 (1.1, 5.0)	0.614
Mother's Age at Enrollment	302	30.8 (30.3, 31.4)	31 (18, 46)	84	29.8 (28.7, 30.9)	31 (15, 38)	0.085
Mother's IQ	302	98.3 (96.8, 99.7)	100 (58, 124)	84	104.6 (101.7, 107.5)	106 (72, 131)	<.001
Father's IQ^b	204	104.1 (102.3, 106.0)	105 (58, 139)	46	104.0 (99.8, 108.2)	102 (75, 136)	0.947
Maternal Relative's IQ^b	111	100.8 (97.8, 103.8)	102 (51, 133)	29	103.0 (98.7, 107.3)	103 (74, 125)	0.493
Beck Depression Inventory-2 (BDI)^c							
Enrollment - 2YO Visit	301	6.31 (5.72, 6.90)	5.3 (0.0, 36.8)	84	5.12 (4.29, 5.95)	4.7 (0.0, 24.0)	0.088
Pregnancy	302	7.09 (6.45, 7.73)	5.7 (0.0, 38.7)	84	5.90 (5.03, 6.77)	5.0 (0.0, 17.7)	0.112
Post-Birth	301	5.83 (5.18, 6.47)	4.5 (0.0, 35.6)	84	4.53 (3.57, 5.50)	3.7 (0.0, 29.0)	0.060
Beck Anxiety Inventory (BAI)^c							
Enrollment - 2YO Visit	301	5.19 (4.65, 5.74)	3.8 (0.0, 34.1)	84	3.54 (2.69, 4.39)	2.7 (0.0, 26.0)	<.001

	Children of WWE, N = 302			Children of WWoE, N = 84			P-Value ^a
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)	
Pregnancy	302	6.41 (5.75, 7.06)	4.8 (0.0, 38.3)	84	4.94 (3.94, 5.94)	3.4 (0.0, 29.3)	0.033
Post-Birth	301	4.41 (3.87, 4.96)	3.0 (0.0, 31.6)	84	2.62 (1.78, 3.45)	1.5 (0.0, 23.5)	<.001
Perceived Stress Scale-14 (PSS)^c							
Enrollment - 2YO Visit	301	17.88 (17.12, 18.63)	17.6 (3.3, 40.6)	84	16.88 (15.77, 17.98)	17.2 (6.4, 29.1)	0.324
Pregnancy	302	17.96 (17.15, 18.78)	17.7 (2.7, 40.0)	84	16.33 (15.02, 17.64)	15.7 (3.3, 30.5)	0.092
Post-Birth	301	17.83 (17.03, 18.64)	17.6 (2.0, 41.0)	84	17.16 (15.97, 18.35)	16.9 (6.2, 33.0)	0.535
Pittsburgh Sleep Quality Index (PSQI)^{bd}							
Pregnancy +Postpartum	237	5.74 (5.41, 6.07)	5.6 (0.1, 13.7)	64	5.25 (4.65, 5.85)	5.0 (1.0, 12.3)	0.171
Pregnancy	276	5.76 (5.41, 6.12)	5.3 (0.0, 15.5)	75	4.70 (4.12, 5.28)	4.3 (1.0, 11.8)	0.005
Postpartum	240	5.69 (5.35, 6.03)	5.4 (0.0, 13.6)	64	5.64 (4.94, 6.34)	5.8 (0.3, 12.5)	0.890

WGA = weeks gestational age

^a P-Values from T-Test (WGA at Birth, WGA at Enrollment, Birthweight, Age, IQ Scores, PSQI Scores) and Wilcoxon Rank-Sum Test (BDI, BAI, and PSS Scores).

^b Father's IQ, Maternal Relative's IQ, and PSQI Scores not assessed for inclusion in imputation model due to extensive missing data.

^c Average of all assessments completed during time period. Enrollment - 2YO Visit: enrollment through 2YO visit; Pregnancy: enrollment through day of delivery; Post-Birth: post-delivery through 2YO visit.

^d Weighted monthly average of PSQI assessments completed during time period. At most one PSQI score per day was used in the calculation. Pregnancy: Enrollment through the day before delivery; Postpartum: 6 weeks

	Children of WWE, N = 302			Children of WWoE, N = 84			
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)	P-Value ^a

through 9 months post-delivery; Pregnancy+Postpartum: Assessments completed during either period (only women with scores in both periods included).

eTable 6. Demographic, Baseline Characteristics, and Risk Factors for Children of WWE and Mothers with Max Observed Ratio ASM Concentration in 3rd Trimester, Categorical Variables, Children in Primary Analysis 2, N = 271

	N = 271
	n (%)
Child's Sex	
Female	143 (52.8)
Male	128 (47.2)
Child's Race	
White	223 (82.3)
Black or African American	11 (4.1)
Other/Unknown	37 (13.7)
Child's Ethnicity - Hispanic or Latino	54 (19.9)
Twin	19 (7.0)
Small for Gestational Age (SGA)	15 (5.7)
Missing	6
Major Congenital Malformations	13 (4.8)
Any Breastfeeding	208 (77.0)
Missing	1
Periconceptual Folate Use	239 (88.2)
Periconceptual Folate Dose	
0 mg	32 (11.9)
> 0 - 0.4 mg	19 (7.0)
> 0.4 - 1 mg	51 (18.9)
> 1 - 4 mg	146 (54.1)
> 4 mg	22 (8.1)
Missing	1

	N = 271
	n (%)
Pregnancy Planned/Welcomed	
Planned	200 (73.8)
Unplanned/Welcome	63 (23.2)
Unplanned/Unwelcome	8 (3.0)
Major Depressive Episode During Pregnancy^a	11 (4.1)
Mother's Education	
College Degree (Advanced)	75 (27.7)
College Degree (Not Advanced)	126 (46.5)
No College Degree	70 (25.8)
Mother's Employment	
Employed full-time	158 (58.3)
Employed part-time	41 (15.1)
Unemployed ^b	72 (26.6)
Household Income	
Subject desires not to answer	11 (4.1)
\$24,999 or less	45 (16.6)
\$25,000-49,999	28 (10.3)
\$50,000-74,999	37 (13.7)
\$75,000-99,999	48 (17.7)
\$100,000 and up	102 (37.6)
Smoking^c	14 (5.2)
Alcohol Use^c	64 (23.6)
Illicit Substance Use^c	8 (3.0)
Missing	1
McMaster FAD Problematic Family Functioning at Child's 2YO Visit	48 (18.7)

	N = 271
	n (%)
Missing	14
Lifetime History of Mood Disorder^d	41 (15.4)
Missing	4
Lifetime History of Anxiety Disorder^d	39 (14.6)
Missing	4
Seizure Type^e	
Focal	164 (60.5)
Generalized	87 (32.1)
Unclassified/Mixed	20 (7.4)
5 or More Convulsions During Pregnancy	9 (3.3)
Missing	1

FAD = Family Assessment Device

Note: Missing not used in calculation of percentages.

^a Depression based on SCID Mood Module at any depression assessment during pregnancy.

^b Unemployed includes stay at home parent without outside job, unemployed due to disability, full-time student and looking for work.

^c Self-reported smoking, alcohol use, or illicit substance use (including marijuana) at any time during pregnancy.

^d Diagnosis from SCID.

^e Three children had mothers who reported multiple seizure types, 2 reported generalized & focal seizures and 1 reported generalized & unclassified seizures.

eTable 7. Demographic, Baseline Characteristics, and Risk Factors for Children of WWE and Mothers With Max Observed Ratio ASM Concentration in 3rd Trimester, Continuous Variables, Children in Primary Analysis 2, N = 271

	N	Mean (95% CI)	Median (Min, Max)
WGA at Birth	271	38.6 (38.4, 38.8)	39 (33, 42)
WGA at Enrollment	271	13.4 (12.8, 13.9)	14 (4, 29)
Birthweight (kg)	266	3.27 (3.20, 3.33)	3.3 (1.7, 4.9)
Mother's Age at Enrollment	271	31.0 (30.4, 31.6)	31 (18, 46)
Mother's IQ	271	98.8 (97.3, 100.3)	100 (65, 124)
Father's IQ^a	189	104.6 (102.7, 106.6)	105 (58, 139)
Maternal Relative's IQ^a	100	101.5 (98.4, 104.7)	104 (51, 133)
Beck Depression Inventory-2 (BDI)^b			
Enrollment - 2YO Visit	270	6.11 (5.49, 6.73)	5.1 (0.0, 36.8)
Pregnancy	271	6.91 (6.22, 7.60)	5.3 (0.0, 38.7)
Post-Birth	270	5.61 (4.95, 6.26)	4.4 (0.0, 35.6)
Beck Anxiety Inventory (BAI)^b			
Enrollment - 2YO Visit	270	5.01 (4.43, 5.58)	3.5 (0.0, 34.1)
Pregnancy	271	6.18 (5.50, 6.86)	4.7 (0.0, 38.3)
Post-Birth	270	4.24 (3.67, 4.81)	2.7 (0.0, 31.6)
Perceived Stress Scale-14 (PSS)^b			
Enrollment - 2YO Visit	270	17.67 (16.87, 18.46)	17.2 (3.3, 40.6)
Pregnancy	271	17.71 (16.84, 18.58)	17.3 (2.7, 40.0)
Post-Birth	270	17.65 (16.80, 18.50)	17.5 (2.0, 41.0)
Pittsburgh Sleep Quality Index (PSQI)^{ac}			
Pregnancy+Postpartum	213	5.71 (5.36, 6.06)	5.6 (0.1, 13.7)
Pregnancy	248	5.69 (5.31, 6.06)	5.1 (0.0, 15.5)
Postpartum	215	5.66 (5.30, 6.02)	5.3 (0.0, 13.6)
Convulsions During Pregnancy	270	0.6 (0.3, 0.9)	0 (0, 28)

	N	Mean (95% CI)	Median (Min, Max)
Max Observed Ratio ASM Concentration^d During 3rd Trimester	271	0.52 (0.48, 0.56)	0.4 (0.0, 1.9)
Max Ratio DDD^e During 3rd Trimester	271	2.21 (2.05, 2.38)	2.0 (0.2, 8.3)

WGA = weeks gestational age

^a Father's IQ, Maternal Relative's IQ, and PSQI Scores not assessed for inclusion in imputation model due to extensive missing data.

^b Average of all assessments completed during time period. Enrollment - 2YO Visit: enrollment through 2YO visit; Pregnancy: enrollment through day of delivery; Post-Birth: post-delivery through 2YO visit.

^c Weighted monthly average of PSQI assessments completed during time period. At most one PSQI score per day was used in the calculation. Pregnancy: Enrollment through the day before delivery; Postpartum: 6 weeks through 9 months post-delivery; Pregnancy+Postpartum: Assessments completed during either period (only women with scores in both periods included).

^d Ratio ASM Concentration calculated as ratio upper limit for therapeutic range. For mothers on polytherapy, ratio ASM Concentration calculated by summing the ratio ASM Concentration for each ASM. Maximum observed value recorded during 3rd trimester, including day of delivery.

^e Ratio DDD = Ratio Defined Daily Dose, calculated by dividing the mother's ASM total prescribed daily dose by the WHO defined daily dose values. For mothers on polytherapy, ratio DDD equals the sum across the ratio DDD for all ASMs.

eTable 8. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Maximum Observed Ratio ASM Concentration^a During 3rd Trimester by ASM Category, Children of WWE With 3rd Trimester Blood Levels, Completers Population

3rd Trimester ASM Category ^d	Unadjusted Analysis ^b			Adjusted Analysis ^c		
	N	Parameter Estimate (95% CI)	P-value	N	Parameter Estimate (95% CI)	P-value
Lamotrigine	79	-11.0 (-24.1, 2.1)	0.101	77	-12.0 (-23.7, -0.3)	0.044
Levetiracetam	70	-16.5 (-25.2, -7.8)	<.001	63	-18.9 (-26.8, -10.9)	<.001
Other Monotherapy	31	7.6 (-10.0, 25.2)	0.396	30	8.3 (-7.7, 24.2)	0.307
Lamotrigine+Levetiracetam	24	-3.6 (-15.3, 8.1)	0.547	22	-1.5 (-13.9, 10.8)	0.808
Other Polytherapy	25	-11.5 (-24.8, 1.8)	0.091	25	-11.5 (-23.6, 0.5)	0.061

Notes: N = children of WWE with Age 4.5 ABAS-3 General Adaptive Composite Score and mother with max observed ratio ASM concentration in 3rd trimester.

12 children were excluded from the adjusted analysis due to missing covariates.

^a Ratio ASM Concentration calculated as ratio upper limit for therapeutic range. For mothers on polytherapy, ratio ASM concentration calculated by summing the ratio ASM concentration for each ASM. Maximum observed value recorded during 3rd trimester, including day of delivery.

^b Linear regression model with Mother's ASM blood levels, ASM Category, and their interaction. P-value for interaction term: 0.128

^c Linear regression model with Mother's ASM blood levels, ASM Category, and their interaction, mother's IQ, education level, age at enrollment, smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status. Mother's ASM group was not included as a covariate in model. P-value for interaction term: 0.022

^d Based on ASM regimen taken at time of blood draw for maximum observed ratio ASM concentration during 3rd trimester (includes day of delivery).

eTable 9. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Maximum Observed Ratio ASM Concentration^a During 3rd Trimester by ASM Group, Children of WWE With 3rd Trimester Blood Levels, Completers Population

3rd Trimester ASM Group ^d	Unadjusted Analysis ^b			Adjusted Analysis ^c		
	N	Parameter Estimate (95% CI)	P-value	N	Parameter Estimate (95% CI)	P-value
Monotherapy	180	-9.6 (-16.0, -3.2)	0.003	170	-10.7 (-16.6, -4.8)	<.001
Polytherapy	49	-7.6 (-16.5, 1.2)	0.091	47	-6.9 (-15.6, 1.9)	0.122

Notes: N = children of WWE with Age 4.5 ABAS-3 General Adaptive Composite Score and mother with max observed ratio ASM Concentration in 3rd trimester.

12 children were excluded from the adjusted analysis due to missing covariates.

^a Ratio ASM Concentration calculated as ratio upper limit for therapeutic range. For mothers on polytherapy, ratio ASM concentration calculated by summing the ratio ASM concentration for each ASM. Maximum observed value recorded during 3rd trimester, including day of delivery.

^b Linear regression model with Mother's ASM blood levels, ASM Group, and their interaction. P-value for interaction term: 0.720

^c Linear regression model with Mother's ASM blood levels, ASM Group, and their interaction, mother's IQ, education level, age at enrollment, smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status. P-value for interaction term: 0.484

^d Based on ASM regimen taken at time of blood draw for maximum observed ratio ASM concentration during 3rd trimester (includes day of delivery).

eTable 10. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Mother's Maximum Ratio DDD^a During 3rd Trimester, Children of WWE on ASM in 3rd Trimester, Completers Population

	Unadjusted Analysis ^b			Adjusted Analysis ^c		
	N	Parameter Estimate (95% CI)	P-value	N	Parameter Estimate (95% CI)	P-value
3rd Trimester Max Ratio DDD ^a	239	-1.99 (-2.89, -1.08)	<.001	226	-1.94 (-3.07, -0.82)	<.001

Notes: N = children of WWE on ASM during 3rd Trimester with Age 4.5 ABAS-3 General Adaptive Composite Score. 13 children were excluded from the adjusted analysis due to missing covariates.

^a Ratio DDD = Ratio Defined Daily Dose, calculated by dividing the mother's ASM total prescribed daily dose by the WHO defined daily dose values. For mothers on polytherapy, ratio DDD equals the sum across the ratio DDD for all ASMs. Maximum ratio DDD during 3rd trimester used for analysis.

^b Linear regression model.

^c Linear regression model adjusted for mother's IQ, education level, age at enrollment, maximum ratio DDD ASM Group (monotherapy/polytherapy), smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster

FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status.

eTable 11. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Mother’s Maximum Ratio DDD^a During 3rd Trimester by ASM Category, Children of WWE on ASM in 3rd Trimester, Completers Population

3rd Trimester ASM Category ^d	Unadjusted Analysis ^b			Adjusted Analysis ^c		
	N	Parameter Estimate (95% CI)	P-value	N	Parameter Estimate (95% CI)	P-value
Lamotrigine	78	-2.5 (-4.9, -0.1)	0.043	76	-2.2 (-4.4, 0.0)	0.053
Levetiracetam	71	-5.6 (-8.6, -2.6)	<.001	63	-6.6 (-9.4, -3.9)	<.001
Other Monotherapy	33	1.8 (-3.5, 7.2)	0.506	32	3.7 (-1.3, 8.7)	0.144
Lamotrigine+Levetiracetam	24	-1.2 (-5.0, 2.6)	0.528	22	0.0 (-3.8, 3.8)	0.999
Other Polytherapy	33	-1.9 (-3.7, -0.1)	0.039	33	-1.0 (-2.7, 0.7)	0.249

Notes: N = children of WWE on ASM during 3rd Trimester with Age 4.5 ABAS-3 General Adaptive Composite Score. 13 children were excluded from the adjusted analysis due to missing covariates.

^a Ratio DDD = Ratio Defined Daily Dose, calculated by dividing the mother’s ASM total prescribed daily dose by the WHO defined daily dose values. For mothers on polytherapy, ratio DDD equals the sum across the ratio DDD for all ASMs. Maximum ratio DDD during 3rd trimester used for analysis.

^b Linear regression model with Mother’s max ratio DDD, ASM Category, and their interaction. P-value for interaction term: 0.111

^c Linear regression model with Mother’s max ratio DDD, ASM Category, and their interaction, mother’s IQ, education level, age at enrollment, smoking during pregnancy, post-birth average BAI score through child’s 2YO visit, McMaster FAD problematic family functioning at child’s 2YO Visit, and child’s sex and small for gestational age status. Mother’s ASM group was not included as a covariate in model. P-value for interaction term: 0.002

^d Based on prescribed ASM regimen at time of max ratio DDD during 3rd trimester.

eTable 12. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Mother's Maximum Ratio DDD^a During 3rd Trimester by ASM Group, Children of WWE on ASM in 3rd Trimester, Completers Population

3rd Trimester ASM Group ^d	Unadjusted Analysis ^b			Adjusted Analysis ^c		
	N	Parameter Estimate (95% CI)	P-value	N	Parameter Estimate (95% CI)	P-value
Monotherapy	182	-2.8 (-4.5, -1.1)	0.001	171	-3.0 (-4.5, -1.4)	<.001
Polytherapy	57	-1.8 (-3.4, -0.1)	0.034	55	-0.9 (-2.5, 0.7)	0.278

Notes: N = children of WWE on ASM during 3rd Trimester with Age 4.5 ABAS-3 General Adaptive Composite Score. 13 children were excluded from the adjusted analysis due to missing covariates.

^a Ratio DDD = Ratio Defined Daily Dose, calculated by dividing the mother's ASM total prescribed daily dose by the WHO defined daily dose values. For mothers on polytherapy, ratio DDD equals the sum across the ratio DDD for all ASMs. Maximum ratio DDD during 3rd trimester used for analysis.

^b Linear regression model with Mother's max ratio DDD, ASM Group, and their interaction. P-value for interaction term: 0.388

^c Linear regression model with Mother's max ratio DDD, ASM Group, and their interaction, mother's IQ, education level, age at enrollment, smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status. P-value for interaction term: 0.069

^d Based on prescribed ASM regimen at time of max ratio DDD during 3rd trimester.

eTable 13. Age 4.5 ABAS-3 General Adaptive Composite Score by Breastfeeding Status, Folate Use, and Folate Dose, Children of WWE and WWoE, Completers Population

Risk Factor	Unadjusted Analysis ^a			Adjusted Analysis ^b		
	N	Mean (95% CI)	P-value	N	LS Mean (95% CI)	P-value
Breastfeeding			0.035			0.590
Any	259	101.8 (100.3, 103.3)		255	101.3 (99.9, 102.6)	
None	67	98.3 (95.5, 101.2)		66	100.4 (97.5, 103.2)	
Periconceptual Folate Use			0.005			0.187
Any	274	101.9 (100.5, 103.2)		271	101.5 (100.2, 102.8)	
None	52	96.9 (92.8, 100.9)		50	99.0 (95.7, 102.3)	
Periconceptual Folate Dose (mg)			0.058			0.590
None	52	96.9 (92.8, 100.9)		50	98.8 (95.4, 102.1)	
> 0-0.4	33	100.7 (97.2, 104.2)		33	100.4 (96.6, 104.2)	
> 0.4-1.0	72	101.3 (98.6, 104.0)		71	101.1 (98.5, 103.6)	
> 1.0-4.0	149	102.2 (100.3, 104.1)		147	101.8 (100.0, 103.7)	
> 4.0	17	104.4 (99.7, 109.1)		17	103.2 (97.9, 108.5)	

Notes: N = children with Age 4.5 ABAS-3 General Adaptive Composite Score and mother with non-missing risk factor. 5 children were excluded from adjusted analyses due to missing covariates.

^a Linear regression model.

^b Linear regression model adjusted for mother's study group, IQ, education level, age at enrollment, illicit drug-use during pregnancy, major depressive episode during pregnancy, post-birth average PSS score through child's 2YO visit, and child's sex, birthweight, and small for gestational age status.

eTable 14. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Mother's Sleep Quality (PSQI), Children of WWE and WWoE, Completers Population

Time Period ^c	Unadjusted Analysis ^a			Adjusted Analysis ^b		
	N	Estimate (95% CI)	P-value	N	Estimate (95% CI)	P-value
Pregnancy+Postpartum	260	-0.50 (-1.05, 0.06)	0.080	256	-0.14 (-0.75, 0.47)	0.655
Pregnancy	298	-0.45 (-0.92, 0.02)	0.060	293	-0.13 (-0.62, 0.37)	0.609
Postpartum	262	-0.34 (-0.85, 0.17)	0.195	258	-0.12 (-0.67, 0.43)	0.665

Notes: N = children with Age 4.5 ABAS-3 General Adaptive Composite Score and mother with non-missing PSQI score. Children with missing covariates excluded from adjusted analyses. PSQI = Pittsburgh Sleep Quality Index

^a Linear regression model.

^b Linear regression model adjusted for mother's study group, IQ, education level, age at enrollment, illicit drug-use during pregnancy, major depressive episode during pregnancy, post-birth average PSS score through child's 2YO visit, and child's sex, birthweight, and small for gestational age status.

^c Weighted monthly average of PSQI assessments completed during time period. At most one PSQI score per day was used in the calculation. Pregnancy: Enrollment through the day before delivery; Postpartum: 6 weeks through 9 months post-delivery;

Pregnancy+Postpartum: Assessments completed during either period (only women with scores in both periods included).

eTable 15. Age 4.5 ABAS-3 General Adaptive Composite Score by Breastfeeding Status, Folate Use, and Folate Dose, Children of WWE on ASM in 3rd Trimester, Completers Population

Risk Factor	Unadjusted Analysis ^a			Adjusted Analysis ^b		
	N	Mean (95% CI)	P-value	N	LS Mean (95% CI)	P-value
Breastfeeding			0.024			0.463
Any	180	102.1 (100.4, 103.9)		165	101.6 (99.9, 103.2)	
None	59	98.1 (95.0, 101.2)		52	100.2 (97.1, 103.3)	
Periconceptional Folate Use			0.024			0.862
Any	212	101.8 (100.2, 103.3)		192	101.3 (99.8, 102.8)	
None	27	96.2 (90.6, 101.9)		25	100.9 (96.3, 105.4)	
Periconceptional Folate Dose (mg)			0.073			0.937
None	27	96.2 (90.6, 101.9)		25	100.9 (96.3, 105.5)	
> 0-0.4	17	98.9 (93.6, 104.1)		16	99.2 (93.9, 104.5)	
> 0.4-1.0	41	99.7 (96.3, 103.0)		40	101.1 (97.7, 104.5)	
> 1.0-4.0	137	102.4 (100.3, 104.5)		120	101.6 (99.6, 103.6)	
> 4.0	17	104.4 (99.7, 109.1)		16	101.9 (96.6, 107.1)	

Notes: N = children of WWE with Age 4.5 ABAS-3 General Adaptive Composite Score and mother on ASM in 3rd trimester. 22 children were excluded from adjusted analyses due to missing covariates.

^a Linear regression model.

^b Linear regression model adjusted for mother's 3rd trimester max observed ratio ASM concentration, ASM Group (monotherapy/polytherapy), IQ, education level, age at enrollment, smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status.

eTable 16. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Maternal Sleep Quality (PSQI), Children of WWE on ASM in 3rd Trimester, Completers Population

Time Period ^c	Unadjusted Analysis ^a			Adjusted Analysis ^b		
	N	Estimate (95% CI)	P-value	N	Estimate (95% CI)	P-value
Pregnancy+Postpartum	193	-0.74 (-1.37, -0.11)	0.021	176	-0.22 (-0.87, 0.43)	0.498
Pregnancy	220	-0.58 (-1.12, -0.04)	0.035	201	-0.17 (-0.72, 0.37)	0.536
Postpartum	195	-0.48 (-1.07, 0.11)	0.111	178	-0.11 (-0.70, 0.47)	0.702

Notes: N = children of WWE with Age 4.5 ABAS-3 General Adaptive Composite Score and mother on ASM in 3rd Trimester and with non-missing PSQI score. Children with missing covariates excluded from adjusted analyses. PSQI = Pittsburgh Sleep Quality Index.

^a Linear regression model.

^b Linear regression model adjusted for mother's 3rd trimester max observed ratio ASM concentration, ASM Group (monotherapy/polytherapy), IQ, education level, age at enrollment, smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status.

^c Weighted monthly average of PSQI assessments completed during time period. At most one PSQI score per day was used in the calculation. Pregnancy: Enrollment through the day before delivery; Postpartum: 6 weeks through 9 months post-delivery; Pregnancy+Postpartum: Assessments completed during either period (only women with scores in both periods included).

eTable 17. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Maternal Psychiatric Risk Factors (BDI, BAI, PSS), Children of WWE and WWoE, Completers Population

Assessment/Time Period ^c	Unadjusted Analysis ^a			Adjusted Analysis ^b		
	N	Estimate (95% CI)	P-value	N	Estimate (95% CI)	P-value
Beck Depression Inventory 2 (BDI)						
Enrollment - 2YO Visit	326	-0.38 (-0.64, -0.13)	0.003	321	-0.38 (-0.65, -0.11)	0.006
Pregnancy	326	-0.27 (-0.51, -0.03)	0.028	321	-0.22 (-0.48, 0.04)	0.098
Post-Birth	326	-0.37 (-0.60, -0.14)	0.002	321	-0.38 (-0.62, -0.14)	0.002
Beck Anxiety Inventory (BAI)						
Enrollment - 2YO Visit	326	-0.55 (-0.82, -0.28)	<.001	321	-0.48 (-0.76, -0.19)	0.001
Pregnancy	326	-0.38 (-0.61, -0.15)	0.001	321	-0.29 (-0.53, -0.05)	0.019
Post-Birth	326	-0.56 (-0.83, -0.29)	<.001	321	-0.51 (-0.79, -0.22)	<.001
Perceived Stress Scale 14 (PSS)						
Enrollment - 2YO Visit	326	-0.45 (-0.65, -0.25)	<.001	321	-0.41 (-0.62, -0.21)	<.001
Pregnancy	326	-0.35 (-0.53, -0.17)	<.001	321	-0.31 (-0.50, -0.12)	0.002
Post-Birth	326	-0.42 (-0.60, -0.23)	<.001	321	-0.38 (-0.56, -0.19)	<.001

Notes: N = children with Age 4.5 ABAS-3 General Adaptive Composite Score. 5 children were excluded from adjusted analyses due to missing covariates.

^a Linear regression model.

^b Linear regression model adjusted for mother's study group, IQ, education level, age at enrollment, illicit drug-use during pregnancy, major depressive episode during pregnancy, and child's sex, birthweight, and small for gestational age status. Model was not adjusted for mother's post-birth average PSS score.

^c Average of all assessments completed during time period. Enrollment - 2YO Visit: enrollment through mother's 2YO visit; Pregnancy: enrollment through day of delivery; Post-Birth: post-delivery through 2YO visit.

eTable 18. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Mother Psychiatric Risk Factors (BDI, BAI, PSS), Children of WWE on ASM in 3rd Trimester, Completers Population

Assessment/Time Period ^c	Unadjusted Analysis ^a			Adjusted Analysis ^b		
	N	Estimate (95% CI)	P-value	N	Estimate (95% CI)	P-value
Beck Depression Inventory 2 (BDI)						
Enrollment - 2YO Visit	239	-0.47 (-0.75, -0.20)	<.001	217	-0.18 (-0.45, 0.10)	0.203
Pregnancy	239	-0.32 (-0.58, -0.06)	0.015	217	-0.12 (-0.37, 0.13)	0.353
Post-Birth	239	-0.48 (-0.73, -0.22)	<.001	217	-0.19 (-0.45, 0.07)	0.153
Beck Anxiety Inventory (BAI)						
Enrollment - 2YO Visit	239	-0.61 (-0.91, -0.32)	<.001	217	-0.38 (-0.67, -0.08)	0.013
Pregnancy	239	-0.43 (-0.68, -0.17)	0.001	217	-0.27 (-0.52, -0.01)	0.039
Post-Birth	239	-0.64 (-0.95, -0.34)	<.001	217	-0.38 (-0.68, -0.09)	0.011
Perceived Stress Scale 14 (PSS)						
Enrollment - 2YO Visit	239	-0.50 (-0.72, -0.28)	<.001	217	-0.26 (-0.49, -0.03)	0.027
Pregnancy	239	-0.40 (-0.60, -0.20)	<.001	217	-0.22 (-0.42, -0.01)	0.041
Post-Birth	239	-0.47 (-0.67, -0.26)	<.001	217	-0.22 (-0.44, -0.01)	0.041

Notes: N = children of WWE with Age 4.5 ABAS-3 General Adaptive Composite Score and mother on ASM in 3rd trimester. 22 children were excluded from adjusted analyses due to missing covariates.

^a Linear regression model.

^b Linear regression model adjusted for mother's 3rd trimester max observed ratio ASM concentration, ASM Group (monotherapy/polytherapy), IQ, education level, age at enrollment, smoking during pregnancy, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status. Model was not adjusted for mother's post-birth average BAI score.

^c Average of all assessments completed during time period. Enrollment - 2YO Visit: enrollment through mother's 2YO visit; Pregnancy: enrollment through day of delivery; Post-Birth: post-delivery through 2YO visit

eTable 19. Continuous Behavior Scores by Mother’s Study Group and Child’s Age, Children of WWE vs WWoE, Completers Population

		Unadjusted ^a			Adjusted ^{ab}		
Child's Age	Mother's Study Group	N	LS Mean (95% CI)	P-Value	N	LS Mean (95% CI)	P-Value
ABAS-3 General Adaptive Composite Standard Score							
Age 3	WWE	292	106.5 (105.1, 107.9)	0.409	282	106.6 (105.3, 108.0)	0.405
	WWoE	80	107.7 (105.3, 110.2)		78	107.8 (105.5, 110.2)	
Age 4.5	WWE	253	101.3 (99.8, 102.7)	0.833	248	101.3 (100.0, 102.6)	0.809
	WWoE	73	100.9 (98.2, 103.6)		73	101.0 (98.4, 103.5)	
<i>P-Value for Interaction Term^c</i>		-	-	0.281	-	-	0.278
ABAS-3 Conceptual Composite Standard Score							
Age 3	WWE	293	105.8 (104.3, 107.4)	0.113	283	106.1 (104.7, 107.5)	0.191
	WWoE	81	108.2 (105.7, 110.7)		79	108.0 (105.6, 110.4)	
Age 4.5	WWE	253	101.8 (100.3, 103.3)	0.810	248	102.0 (100.7, 103.3)	0.919
	WWoE	73	102.2 (99.3, 105.1)		73	101.8 (99.1, 104.5)	
<i>P-Value for Interaction Term^c</i>		-	-	0.174	-	-	0.160
ABAS-3 Social Composite Standard Score							
Age 3	WWE	292	107.7 (106.3, 109.2)	0.843	282	107.8 (106.4, 109.2)	0.874
	WWoE	81	108.0 (105.4, 110.6)		79	108.0 (105.5, 110.6)	
Age 4.5	WWE	256	101.7 (100.4, 103.0)	0.918	250	101.7 (100.5, 102.9)	0.883
	WWoE	73	101.5 (98.9, 104.2)		73	101.5 (99.0, 104.0)	
<i>P-Value for Interaction Term^c</i>		-	-	0.783	-	-	0.789
ABAS-3 Practical Composite Standard Score							
Age 3	WWE	293	105.7 (104.2, 107.1)	0.424	283	105.9 (104.5, 107.3)	0.510
	WWoE	80	106.9 (104.4, 109.4)		78	106.8 (104.5, 109.2)	
Age 4.5	WWE	255	102.2 (100.8, 103.6)	0.773	249	102.4 (101.0, 103.7)	0.654
	WWoE	73	101.7 (99.0, 104.5)		73	101.7 (99.2, 104.2)	

		Unadjusted ^a			Adjusted ^{ab}		
Child's Age	Mother's Study Group	N	LS Mean (95% CI)	P-Value	N	LS Mean (95% CI)	P-Value
<i>P-Value for Interaction Term^c</i>		-	-	0.259	-	-	0.265
BASC-2 Hyperactivity Subscale T-Score							
Age 2	WWE	296	49.5 (48.5, 50.5)	0.089	289	49.5 (48.5, 50.5)	0.028
	WwoE	90	47.7 (46.0, 49.5)		88	47.4 (45.7, 49.0)	
Age 3	WWE	291	48.0 (47.0, 49.1)	0.482	282	47.9 (46.9, 49.0)	0.362
	WwoE	83	47.2 (45.3, 49.2)		81	47.0 (45.1, 48.8)	
Age 4.5	WWE	256	48.1 (46.9, 49.3)	0.580	249	48.2 (47.0, 49.4)	0.368
	WwoE	74	47.4 (45.0, 49.7)		74	47.1 (44.9, 49.3)	
<i>P-Value for Interaction Term^c</i>		-	-	0.615	-	-	0.551
BASC-2 Aggression Subscale T-Score							
Age 2	WWE	296	44.6 (43.7, 45.4)	0.976	289	44.5 (43.7, 45.3)	0.747
	WwoE	90	44.6 (43.2, 46.0)		88	44.3 (42.8, 45.7)	
Age 3	WWE	291	45.6 (44.7, 46.5)	0.661	282	45.7 (44.8, 46.6)	0.929
	WwoE	82	46.0 (44.2, 47.9)		80	45.6 (43.8, 47.3)	
Age 4.5	WWE	255	45.7 (44.7, 46.6)	0.845	248	45.8 (44.9, 46.7)	0.721
	WwoE	74	45.9 (44.0, 47.7)		74	45.5 (43.7, 47.2)	
<i>P-Value for Interaction Term^c</i>		-	-	0.920	-	-	0.968
BASC-2 Anxiety Subscale T-Score							
Age 2	WWE	294	44.7 (43.9, 45.6)	0.852	287	44.8 (43.9, 45.6)	0.914
	WwoE	90	44.6 (43.2, 46.0)		88	44.7 (43.2, 46.2)	
Age 3	WWE	290	49.8 (48.7, 50.9)	0.188	281	49.8 (48.7, 50.9)	0.189
	WwoE	83	48.3 (46.4, 50.2)		81	48.3 (46.4, 50.2)	
Age 4.5	WWE	256	48.5 (47.3, 49.7)	0.978	249	48.4 (47.3, 49.6)	0.958
	WwoE	74	48.5 (46.2, 50.8)		74	48.4 (46.1, 50.7)	

		Unadjusted ^a			Adjusted ^{ab}		
Child's Age	Mother's Study Group	N	LS Mean (95% CI)	P-Value	N	LS Mean (95% CI)	P-Value
<i>P-Value for Interaction Term^c</i>		-	-	0.377	-	-	0.362
BASC-2 Depression Subscale T-Score							
Age 2	WWE	296	46.3 (45.4, 47.1)	0.263	289	46.2 (45.4, 47.1)	0.301
	WwoE	90	45.2 (43.6, 46.9)		88	45.3 (43.7, 46.9)	
Age 3	WWE	291	46.3 (45.3, 47.3)	0.714	282	46.3 (45.3, 47.3)	0.729
	WwoE	83	45.9 (44.0, 47.8)		81	45.9 (44.0, 47.8)	
Age 4.5	WWE	256	46.7 (45.5, 47.8)	0.947	249	46.6 (45.4, 47.7)	0.945
	WwoE	74	46.6 (44.0, 49.1)		74	46.5 (44.0, 49.0)	
<i>P-Value for Interaction Term^c</i>		-	-	0.719	-	-	0.779
BASC-2 Somatization Subscale T-Score							
Age 2	WWE	296	46.2 (45.4, 47.1)	0.064	289	46.1 (45.3, 47.0)	0.191
	WwoE	90	44.6 (43.1, 46.1)		88	45.0 (43.4, 46.5)	
Age 3	WWE	291	46.7 (45.8, 47.6)	0.021	282	46.7 (45.8, 47.6)	0.049
	WwoE	83	44.5 (43.0, 46.1)		81	44.9 (43.4, 46.4)	
Age 4.5	WWE	256	45.0 (44.0, 46.1)	0.507	249	45.0 (44.0, 46.0)	0.726
	WwoE	74	44.3 (42.2, 46.3)		74	44.6 (42.5, 46.6)	
<i>P-Value for Interaction Term^c</i>		-	-	0.437	-	-	0.395
BASC-2 Atypicality Subscale T-Score							
Age 2	WWE	295	53.4 (52.4, 54.5)	0.071	288	53.6 (52.6, 54.6)	0.008
	WwoE	90	51.4 (49.4, 53.4)		88	50.8 (49.0, 52.6)	
Age 3	WWE	291	48.1 (47.1, 49.0)	0.399	282	48.3 (47.3, 49.2)	0.130
	WwoE	82	47.2 (45.4, 49.0)		80	46.8 (45.1, 48.5)	
Age 4.5	WWE	255	47.2 (46.2, 48.2)	0.995	248	47.4 (46.4, 48.5)	0.625
	WwoE	74	47.2 (44.8, 49.6)		74	46.8 (44.5, 49.1)	

		Unadjusted ^a			Adjusted ^{ab}		
Child's Age	Mother's Study Group	N	LS Mean (95% CI)	P-Value	N	LS Mean (95% CI)	P-Value
<i>P-Value for Interaction Term^c</i>		-	-	0.302	-	-	0.237
BASC-2 Withdrawal Subscale T-Score							
Age 2	WWE	295	50.1 (49.2, 51.0)	0.698	288	49.9 (49.0, 50.9)	0.537
	WwoE	90	50.5 (48.9, 52.0)		88	50.5 (48.9, 52.1)	
Age 3	WWE	290	46.9 (46.0, 47.9)	0.205	281	46.8 (45.9, 47.8)	0.125
	WwoE	83	48.4 (46.3, 50.4)		81	48.6 (46.6, 50.5)	
Age 4.5	WWE	255	47.3 (46.2, 48.4)	0.969	248	47.4 (46.3, 48.4)	0.988
	WwoE	74	47.3 (45.0, 49.5)		74	47.3 (45.1, 49.6)	
<i>P-Value for Interaction Term^c</i>		-	-	0.360	-	-	0.277
BASC-2 Attention Problems Subscale T-Score							
Age 2	WWE	296	50.9 (49.9, 51.8)	0.077	289	50.9 (49.9, 51.9)	0.030
	WwoE	90	49.0 (47.2, 50.8)		88	48.6 (46.8, 50.4)	
Age 3	WWE	291	47.4 (46.4, 48.4)	0.937	282	47.5 (46.5, 48.4)	0.720
	WwoE	83	47.4 (45.7, 49.0)		81	47.1 (45.4, 48.8)	
Age 4.5	WWE	256	48.5 (47.4, 49.6)	0.071	249	48.5 (47.5, 49.5)	0.034
	WwoE	74	46.4 (44.3, 48.4)		74	46.1 (44.1, 48.1)	
<i>P-Value for Interaction Term^c</i>		-	-	0.075	-	-	0.065
BASC-2 Adaptability Subscale T-Score							
Age 2	WWE	296	51.0 (50.0, 52.0)	0.909	289	51.3 (50.3, 52.2)	0.387
	WwoE	90	50.8 (49.0, 52.7)		88	50.3 (48.5, 52.2)	
Age 3	WWE	291	54.2 (53.0, 55.3)	0.015	282	54.3 (53.3, 55.4)	0.003
	WwoE	83	51.5 (49.8, 53.3)		81	51.0 (49.1, 52.9)	
Age 4.5	WWE	256	52.9 (51.6, 54.1)	0.610	249	53.2 (52.0, 54.4)	0.928
	WwoE	74	53.6 (51.3, 55.9)		74	53.1 (50.7, 55.4)	

		Unadjusted ^a			Adjusted ^{ab}		
Child's Age	Mother's Study Group	N	LS Mean (95% CI)	P-Value	N	LS Mean (95% CI)	P-Value
<i>P-Value for Interaction Term^c</i>		-	-	0.007	-	-	0.011
BASC-2 Social Skills Subscale T-Score							
Age 2	WWE	296	44.9 (44.0, 45.8)	0.731	289	44.9 (44.0, 45.8)	0.735
	WWoE	90	45.2 (43.4, 47.0)		88	45.2 (43.4, 47.1)	
Age 3	WWE	291	54.4 (53.4, 55.4)	0.273	282	54.4 (53.4, 55.4)	0.298
	WWoE	83	53.3 (51.6, 55.0)		81	53.3 (51.6, 55.1)	
Age 4.5	WWE	256	54.8 (53.5, 56.0)	0.143	249	54.8 (53.6, 56.0)	0.122
	WWoE	74	56.5 (54.5, 58.6)		74	56.6 (54.7, 58.6)	
<i>P-Value for Interaction Term^c</i>		-	-	0.015	-	-	0.015

N = children with non-missing behavior score. Children with missing covariates excluded from adjusted model.

^a LS Means and P-Value from a longitudinal generalized linear model with identity link function and generalized estimating equations and unstructured covariance structure including mother's study group, child's age, and their interaction.

^b Adjusted for IQ, education level, age at enrollment, illicit drug-use during pregnancy, major depressive episode during pregnancy, post-birth average PSS score through child's 2YO visit, and child's sex, birthweight, and small for gestational age status.

^c P-value for the interaction between mother's study group and child's age calculated using the Score test. If significant, the association between the mother's study group and behavior score differs among child's age.

eTable 20. Association Between Continuous Behavior Scores and Maximum Observed Ratio ASM Concentration^a in 3rd Trimester by Child's Age, Children of WWE With 3rd Trimester Blood Levels, Completers Population

Child's Age	Unadjusted ^b			Adjusted ^{bc}		
	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
ABAS-3 General Adaptive Composite Standard Score						
Age 3	261	-4.7 (-9.1, -0.2)	0.040	245	-3.9 (-9.9, 2.2)	0.211
Age 4.5	229	-7.8 (-12.1, -3.4)	<.001	217	-7.1 (-13.1, -1.1)	0.021
<i>P-Value for Interaction Term^d</i>	-	-	0.086	-	-	0.085
ABAS-3 Conceptual Composite Standard Score						
Age 3	262	-5.4 (-10.4, -0.5)	0.031	246	-4.0 (-10.8, 2.7)	0.238
Age 4.5	229	-6.5 (-11.0, -2.0)	0.005	217	-5.1 (-11.6, 1.3)	0.117
<i>P-Value for Interaction Term^d</i>	-	-	0.563	-	-	0.563
ABAS-3 Social Composite Standard Score						
Age 3	261	-4.3 (-9.0, 0.5)	0.079	245	-3.4 (-9.4, 2.7)	0.276
Age 4.5	232	-8.0 (-12.0, -4.1)	<.001	219	-7.6 (-12.9, -2.3)	0.005
<i>P-Value for Interaction Term^d</i>	-	-	0.064	-	-	0.044
ABAS-3 Practical Composite Standard Score						
Age 3	262	-3.8 (-8.2, 0.6)	0.088	246	-3.8 (-9.7, 2.0)	0.201
Age 4.5	231	-7.4 (-11.7, -3.1)	<.001	218	-7.5 (-13.4, -1.6)	0.013
<i>P-Value for Interaction Term^d</i>	-	-	0.049	-	-	0.053
BASC-2 Hyperactivity Subscale T-Score						
Age 2	265	3.7 (0.7, 6.7)	0.014	256	3.6 (0.0, 7.1)	0.047
Age 3	260	2.0 (-1.0, 5.1)	0.190	245	1.5 (-2.1, 5.2)	0.412
Age 4.5	232	4.7 (0.7, 8.7)	0.022	218	4.1 (-0.6, 8.8)	0.089
<i>P-Value for Interaction Term^d</i>	-	-	0.275	-	-	0.251
BASC-2 Aggression Subscale T-Score						

Child's Age	Unadjusted ^b			Adjusted ^{bc}		
	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
Age 2	265	2.2 (-0.1, 4.4)	0.060	256	1.9 (-0.8, 4.7)	0.173
Age 3	260	3.0 (0.7, 5.4)	0.012	245	2.8 (-0.1, 5.7)	0.059
Age 4.5	232	3.7 (1.1, 6.3)	0.006	218	3.5 (0.3, 6.8)	0.032
<i>P-Value for Interaction Term^d</i>	-	-	0.507	-	-	0.505
BASC-2 Anxiety Subscale T-Score						
Age 2	263	-0.9 (-3.4, 1.5)	0.461	254	-1.1 (-4.3, 2.1)	0.493
Age 3	259	0.0 (-3.3, 3.4)	0.977	244	-0.3 (-4.3, 3.7)	0.883
Age 4.5	232	1.3 (-1.8, 4.4)	0.425	218	1.6 (-2.2, 5.5)	0.405
<i>P-Value for Interaction Term^d</i>	-	-	0.385	-	-	0.216
BASC-2 Depression Subscale T-Score						
Age 2	265	1.5 (-1.0, 3.9)	0.250	256	1.0 (-2.4, 4.4)	0.569
Age 3	260	0.7 (-2.3, 3.7)	0.634	245	0.0 (-3.8, 3.8)	0.990
Age 4.5	232	3.7 (0.2, 7.2)	0.039	218	3.1 (-1.4, 7.6)	0.174
<i>P-Value for Interaction Term^d</i>	-	-	0.190	-	-	0.190
BASC-2 Somatization Subscale T-Score						
Age 2	265	0.5 (-2.4, 3.4)	0.734	256	0.1 (-3.6, 3.8)	0.957
Age 3	260	0.5 (-2.6, 3.6)	0.770	245	-0.7 (-4.7, 3.3)	0.746
Age 4.5	232	0.3 (-3.2, 3.7)	0.878	218	-0.8 (-4.9, 3.2)	0.694
<i>P-Value for Interaction Term^d</i>	-	-	0.987	-	-	0.786
BASC-2 Atypicality Subscale T-Score						
Age 2	264	1.9 (-0.9, 4.8)	0.188	255	1.9 (-1.3, 5.1)	0.246
Age 3	260	3.5 (0.5, 6.6)	0.024	245	3.4 (-0.3, 7.1)	0.069
Age 4.5	232	3.5 (0.1, 7.0)	0.044	218	2.6 (-1.6, 6.8)	0.221
<i>P-Value for Interaction Term^d</i>	-	-	0.604	-	-	0.653

Child's Age	Unadjusted ^b			Adjusted ^{bc}		
	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
BASC-2 Withdrawal Subscale T-Score						
Age 2	264	-0.4 (-3.0, 2.2)	0.782	255	0.1 (-2.9, 3.1)	0.961
Age 3	259	1.0 (-1.8, 3.8)	0.497	244	1.3 (-2.1, 4.7)	0.460
Age 4.5	232	1.9 (-1.2, 5.1)	0.230	218	2.3 (-1.7, 6.4)	0.261
<i>P-Value for Interaction Term^d</i>	-	-	0.480	-	-	0.529
BASC-2 Attention Problems Subscale T-Score						
Age 2	265	1.1 (-1.8, 4.0)	0.455	256	0.8 (-2.8, 4.4)	0.656
Age 3	260	2.6 (-0.6, 5.7)	0.107	245	2.1 (-2.0, 6.2)	0.308
Age 4.5	232	2.9 (-0.4, 6.2)	0.081	218	2.3 (-1.8, 6.3)	0.272
<i>P-Value for Interaction Term^d</i>	-	-	0.544	-	-	0.669
BASC-2 Adaptability Subscale T-Score						
Age 2	265	-2.4 (-5.5, 0.6)	0.116	256	-1.5 (-5.1, 2.0)	0.396
Age 3	260	-4.6 (-8.0, -1.1)	0.009	245	-3.3 (-7.3, 0.7)	0.102
Age 4.5	232	-3.6 (-7.5, 0.3)	0.068	218	-2.7 (-7.3, 1.9)	0.255
<i>P-Value for Interaction Term^d</i>	-	-	0.534	-	-	0.670
BASC-2 Social Skills Subscale T-Score						
Age 2	265	-2.5 (-5.4, 0.4)	0.094	256	-2.3 (-6.2, 1.5)	0.238
Age 3	260	-3.9 (-7.0, -0.8)	0.014	245	-3.9 (-8.0, 0.1)	0.057
Age 4.5	232	-4.8 (-8.7, -1.0)	0.014	218	-5.1 (-9.9, -0.3)	0.038
<i>P-Value for Interaction Term^d</i>	-	-	0.458	-	-	0.377

Child's Age	Unadjusted ^b			Adjusted ^{bc}		
	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value

N = children of WWE with non-missing behavior score and mothers with max observed ratio ASM Concentration in 3rd

trimester (includes day of delivery). Children with missing covariates excluded from adjusted model.

^a Ratio ASM Concentration calculated as ratio upper limit for therapeutic range. For mothers on polytherapy, ratio ASM concentration calculated by summing the ratio ASM concentration for each ASM.

Maximum observed value recorded during 3rd trimester, including day of delivery.

^b Parameter Estimate and P-Value from a longitudinal generalized linear model with identity link function and generalized estimating equations and unstructured covariance structure including mother's max observed ratio ASM concentration in 3rd trimester, child's age, and their interaction.

^c Adjusted for mother's IQ, education level, age at enrollment, ASM group (Monotherapy/Polytherapy), smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status.

^d P-value for the interaction between max observed ratio ASM concentration in 3rd trimester and child's age calculated using the Score test. If significant, the association between max observed ratio ASM concentration in 3rd trimester and behavior score differs among child's age.

eTable 21. Association Between Continuous Behavior Scores and Maximum Ratio DDD^a in 3rd Trimester by Child's Age, Children of WWE on ASM in 3rd Trimester, Completers Population

Child's Age	Unadjusted ^b			Adjusted ^{bc}		
	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
ABAS-3 General Adaptive Composite Standard Score						
Age 3	278	-1.8 (-2.6, -1.0)	<.001	260	-1.7 (-2.8, -0.6)	0.002
Age 4.5	239	-1.8 (-2.5, -1.1)	<.001	226	-1.7 (-2.7, -0.7)	0.001
<i>P-Value for Interaction Term^d</i>	-	-	>.999	-	-	0.929
ABAS-3 Conceptual Composite Standard Score						
Age 3	279	-2.2 (-3.1, -1.3)	<.001	261	-1.7 (-2.8, -0.5)	0.004
Age 4.5	239	-1.7 (-2.5, -0.9)	<.001	226	-1.2 (-2.3, -0.2)	0.021
<i>P-Value for Interaction Term^d</i>	-	-	0.230	-	-	0.253
ABAS-3 Social Composite Standard Score						
Age 3	278	-1.8 (-2.8, -0.8)	<.001	260	-1.6 (-2.8, -0.4)	0.011
Age 4.5	242	-2.0 (-2.7, -1.2)	<.001	228	-1.7 (-2.7, -0.8)	<.001
<i>P-Value for Interaction Term^d</i>	-	-	0.745	-	-	0.730
ABAS-3 Practical Composite Standard Score						
Age 3	279	-1.4 (-2.3, -0.6)	<.001	261	-1.6 (-2.6, -0.5)	0.004
Age 4.5	241	-1.4 (-2.3, -0.5)	0.002	227	-1.5 (-2.7, -0.3)	0.018
<i>P-Value for Interaction Term^d</i>	-	-	0.940	-	-	0.879
BASC-2 Hyperactivity Subscale T-Score						
Age 2	282	1.2 (0.4, 2.1)	0.005	272	1.1 (0.2, 2.1)	0.022
Age 3	277	1.1 (0.3, 1.8)	0.006	260	0.9 (0.1, 1.8)	0.037
Age 4.5	242	1.1 (0.2, 2.1)	0.018	227	0.9 (-0.1, 1.9)	0.084
<i>P-Value for Interaction Term^d</i>	-	-	0.870	-	-	0.809
BASC-2 Aggression Subscale T-Score						

Child's Age	Unadjusted ^b			Adjusted ^{bc}		
	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
Age 2	282	0.7 (-0.1, 1.5)	0.076	272	0.6 (-0.3, 1.5)	0.166
Age 3	277	0.8 (0.0, 1.6)	0.061	260	0.7 (-0.2, 1.5)	0.133
Age 4.5	242	0.4 (-0.1, 0.9)	0.101	227	0.2 (-0.4, 0.8)	0.460
<i>P-Value for Interaction Term^d</i>	-	-	0.604	-	-	0.486
BASC-2 Anxiety Subscale T-Score						
Age 2	280	-0.1 (-0.8, 0.5)	0.704	270	-0.2 (-1.0, 0.6)	0.674
Age 3	276	-0.2 (-0.9, 0.5)	0.602	259	-0.3 (-1.1, 0.5)	0.469
Age 4.5	242	-0.4 (-1.1, 0.3)	0.291	227	-0.4 (-1.4, 0.5)	0.329
<i>P-Value for Interaction Term^d</i>	-	-	0.846	-	-	0.854
BASC-2 Depression Subscale T-Score						
Age 2	282	0.8 (0.1, 1.6)	0.037	272	0.9 (-0.1, 1.8)	0.070
Age 3	277	0.6 (-0.2, 1.3)	0.128	260	0.6 (-0.3, 1.4)	0.197
Age 4.5	242	0.7 (0.1, 1.3)	0.030	227	0.7 (-0.1, 1.4)	0.072
<i>P-Value for Interaction Term^d</i>	-	-	0.652	-	-	0.592
BASC-2 Somatization Subscale T-Score						
Age 2	282	0.0 (-0.6, 0.5)	0.905	272	-0.1 (-0.7, 0.5)	0.785
Age 3	277	0.1 (-0.5, 0.7)	0.746	260	0.0 (-0.7, 0.7)	0.934
Age 4.5	242	-0.3 (-0.9, 0.3)	0.390	227	-0.4 (-1.1, 0.3)	0.300
<i>P-Value for Interaction Term^d</i>	-	-	0.687	-	-	0.662
BASC-2 Atypicality Subscale T-Score						
Age 2	281	0.8 (0.1, 1.5)	0.022	271	0.6 (-0.1, 1.4)	0.114
Age 3	277	0.6 (-0.1, 1.3)	0.101	260	0.3 (-0.5, 1.1)	0.422
Age 4.5	242	0.5 (-0.2, 1.1)	0.154	227	0.1 (-0.6, 0.9)	0.742
<i>P-Value for Interaction Term^d</i>	-	-	0.718	-	-	0.515

Child's Age	Unadjusted ^b			Adjusted ^{bc}		
	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
BASC-2 Withdrawal Subscale T-Score						
Age 2	281	-0.4 (-1.0, 0.3)	0.257	271	-0.3 (-1.0, 0.5)	0.498
Age 3	276	0.4 (-0.5, 1.2)	0.413	259	0.4 (-0.5, 1.4)	0.363
Age 4.5	242	0.4 (-0.3, 1.1)	0.271	227	0.4 (-0.4, 1.2)	0.297
<i>P-Value for Interaction Term^d</i>	-	-	0.208	-	-	0.256
BASC-2 Attention Problems Subscale T-Score						
Age 2	282	0.6 (-0.1, 1.3)	0.100	272	0.4 (-0.4, 1.3)	0.318
Age 3	277	0.8 (0.1, 1.4)	0.023	260	0.6 (-0.2, 1.4)	0.153
Age 4.5	242	0.8 (0.0, 1.6)	0.038	227	0.6 (-0.2, 1.4)	0.168
<i>P-Value for Interaction Term^d</i>	-	-	0.864	-	-	0.922
BASC-2 Adaptability Subscale T-Score						
Age 2	282	-0.4 (-1.1, 0.3)	0.236	272	0.0 (-0.8, 0.8)	0.916
Age 3	277	-0.6 (-1.4, 0.2)	0.150	260	-0.2 (-1.2, 0.7)	0.664
Age 4.5	242	-0.2 (-0.9, 0.5)	0.527	227	0.1 (-0.7, 1.0)	0.730
<i>P-Value for Interaction Term^d</i>	-	-	0.558	-	-	0.615
BASC-2 Social Skills Subscale T-Score						
Age 2	282	-0.8 (-1.4, -0.3)	0.002	272	-0.7 (-1.4, 0.0)	0.042
Age 3	277	-1.2 (-1.9, -0.6)	<.001	260	-1.1 (-2.0, -0.3)	0.008
Age 4.5	242	-1.2 (-2.1, -0.3)	0.008	227	-1.1 (-2.1, -0.1)	0.037
<i>P-Value for Interaction Term^d</i>	-	-	0.502	-	-	0.449

Child's Age	Unadjusted ^b			Adjusted ^{bc}		
	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value

N = children of WWE on ASM in 3rd trimester with non-missing behavior score. Children with missing covariates excluded from adjusted model.

^a Ratio DDD = Ratio Defined Daily Dose, calculated by dividing the mother's ASM total prescribed daily dose by the WHO defined daily dose values. For mothers on polytherapy, ratio DDD equals the sum across the ratio DDD for all ASMs. Maximum ratio DDD during 3rd trimester used for analysis.

^b Parameter Estimate and P-Value from a longitudinal generalized linear model with identity link function and generalized estimating equations and unstructured covariance structure including mother's max ratio DDD in 3rd trimester, child's age, and their interaction.

^c Adjusted for mother's IQ, education level, age at enrollment, ASM group (Monotherapy/Polytherapy), smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status.

^d P-value for the interaction between max ratio DDD in 3rd trimester and child's age calculated using the Score test. If significant, the association between max ratio DDD in 3rd trimester and behavior score differs among child's age.

eTable 22. Association Between Continuous Behavior Scores and Maximum Observed Ratio ASM Concentration ^a in 3rd Trimester by ASM Category and Child's Age, Children of WVE with 3rd Trimester Blood Levels, Completers Population

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
ABAS-3 General Adaptive Composite Standard Score							
Age 3	Lamotrigine	93	-3.0 (-16.2, 10.1)	0.651	88	-3.9 (-15.1, 7.2)	0.488
	Levetiracetam	75	-5.0 (-16.4, 6.3)	0.386	68	-7.9 (-18.8, 3.0)	0.156
	Other Monotherapy	42	-7.6 (-30.8, 15.7)	0.525	39	-3.4 (-21.9, 15.1)	0.720
	Lamotrigine+ Levetiracetam	24	-2.3 (-12.0, 7.3)	0.636	23	0.1 (-11.1, 11.3)	0.986
	Other Polytherapy	27	0.6 (-12.4, 13.7)	0.927	27	0.8 (-15.0, 16.6)	0.922
Age 4.5	Lamotrigine	79	-9.0 (-20.5, 2.5)	0.126	77	-10.8 (-20.5, -1.2)	0.028
	Levetiracetam	70	-16.2 (-26.7, -5.8)	0.002	63	-19.4 (-29.0, -9.9)	<.001
	Other Monotherapy	31	9.5 (-17.7, 36.7)	0.493	30	12.5 (-5.8, 30.9)	0.181
	Lamotrigine+ Levetiracetam	24	-3.5 (-11.9, 4.8)	0.407	22	-0.5 (-7.1, 6.1)	0.884
	Other Polytherapy	25	-11.3 (-29.9, 7.3)	0.234	25	-10.9 (-31.3, 9.5)	0.293
<i>P-Value for Interaction Term^e</i>		-	-	0.019	-	-	0.020
ABAS-3 Conceptual Composite Standard Score							
Age 3	Lamotrigine	93	4.2 (-8.2, 16.6)	0.504	88	2.2 (-8.3, 12.6)	0.681
	Levetiracetam	76	-8.2 (-22.4, 6.1)	0.261	69	-10.4 (-23.1, 2.3)	0.108
	Other Monotherapy	42	-8.3 (-33.1, 16.5)	0.512	39	-6.1 (-25.0, 12.8)	0.529
	Lamotrigine+ Levetiracetam	24	1.8 (-8.2, 11.9)	0.720	23	3.9 (-6.4, 14.1)	0.458
	Other Polytherapy	27	4.3 (-9.9, 18.5)	0.553	27	4.2 (-11.5, 19.8)	0.602
Age 4.5	Lamotrigine	79	-5.0 (-16.3, 6.3)	0.387	77	-8.1 (-17.9, 1.6)	0.102
	Levetiracetam	70	-14.6 (-27.5, -1.8)	0.025	63	-17.2 (-28.8, -5.6)	0.004
	Other Monotherapy	31	15.3 (-9.0, 39.7)	0.217	30	16.7 (2.3, 31.2)	0.023

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Lamotrigine+ Levetiracetam	24	-0.9 (-9.5, 7.7)	0.836	22	1.9 (-5.3, 9.1)	0.604
	Other Polytherapy	25	-8.0 (-25.0, 9.0)	0.355	25	-8.0 (-25.8, 9.9)	0.382
<i>P-Value for Interaction Term^e</i>		-	-	0.032	-	-	0.036
ABAS-3 Social Composite Standard Score							
Age 3	Lamotrigine	93	-3.2 (-16.5, 10.1)	0.634	88	-3.7 (-15.1, 7.7)	0.527
	Levetiracetam	75	-5.1 (-16.2, 5.9)	0.362	68	-8.2 (-18.7, 2.4)	0.130
	Other Monotherapy	42	-5.4 (-27.3, 16.5)	0.630	39	-0.5 (-18.4, 17.3)	0.952
	Lamotrigine+ Levetiracetam	24	0.1 (-13.3, 13.5)	0.991	23	-1.3 (-17.1, 14.5)	0.871
	Other Polytherapy	27	-0.2 (-13.4, 13.0)	0.978	27	0.0 (-15.2, 15.3)	0.997
Age 4.5	Lamotrigine	81	-7.8 (-18.3, 2.7)	0.145	79	-9.6 (-19.2, 0.1)	0.051
	Levetiracetam	70	-14.6 (-24.4, -4.8)	0.004	63	-17.7 (-26.4, -9.0)	<.001
	Other Monotherapy	32	-2.0 (-24.9, 21.0)	0.866	30	1.9 (-14.3, 18.1)	0.814
	Lamotrigine+ Levetiracetam	24	1.8 (-3.8, 7.3)	0.537	22	0.2 (-6.5, 7.0)	0.947
	Other Polytherapy	25	-11.5 (-26.6, 3.5)	0.134	25	-11.1 (-27.2, 4.9)	0.174
<i>P-Value for Interaction Term^e</i>		-	-	0.339	-	-	0.410
ABAS-3 Practical Composite Standard Score							
Age 3	Lamotrigine	93	-5.2 (-18.4, 8.0)	0.438	88	-5.5 (-16.5, 5.6)	0.332
	Levetiracetam	76	-5.2 (-15.5, 5.0)	0.318	69	-7.9 (-18.3, 2.5)	0.139
	Other Monotherapy	42	-2.8 (-26.9, 21.4)	0.822	39	1.3 (-17.9, 20.5)	0.891
	Lamotrigine+ Levetiracetam	24	-6.6 (-15.4, 2.1)	0.138	23	-3.1 (-14.1, 8.0)	0.588
	Other Polytherapy	27	-3.9 (-16.7, 8.9)	0.552	27	-3.0 (-18.9, 13.0)	0.716
Age 4.5	Lamotrigine	80	-13.0 (-24.8, -1.2)	0.031	78	-14.1 (-24.3, -4.0)	0.006

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Levetiracetam	70	-16.3 (-25.3, -7.3)	<.001	63	-18.8 (-27.5, -10.2)	<.001
	Other Monotherapy	32	8.5 (-18.7, 35.7)	0.539	30	12.6 (-6.7, 32.0)	0.200
	Lamotrigine+ Levetiracetam	24	-6.8 (-16.0, 2.4)	0.147	22	-2.7 (-11.8, 6.4)	0.555
	Other Polytherapy	25	-10.0 (-28.9, 9.0)	0.303	25	-8.9 (-30.1, 12.2)	0.408
<i>P-Value for Interaction Term^e</i>		-	-	0.022	-	-	0.017
BASC-2 Hyperactivity Subscale T-Score							
Age 2	Lamotrigine	96	6.3 (-2.2, 14.9)	0.147	94	6.2 (-1.8, 14.3)	0.131
	Levetiracetam	71	3.3 (-4.0, 10.6)	0.375	68	4.1 (-3.0, 11.2)	0.255
	Other Monotherapy	44	4.0 (-6.4, 14.5)	0.447	41	5.1 (-3.8, 14.0)	0.263
	Lamotrigine+ Levetiracetam	27	3.1 (-4.7, 10.9)	0.439	26	0.7 (-6.6, 8.1)	0.845
	Other Polytherapy	27	-4.5 (-11.1, 2.1)	0.184	27	-4.3 (-12.3, 3.7)	0.295
Age 3	Lamotrigine	94	5.0 (-3.8, 13.8)	0.264	89	4.8 (-3.7, 13.2)	0.270
	Levetiracetam	74	0.9 (-4.8, 6.7)	0.749	68	2.3 (-3.0, 7.7)	0.391
	Other Monotherapy	41	7.8 (-9.3, 24.9)	0.371	38	8.9 (-6.9, 24.6)	0.270
	Lamotrigine+ Levetiracetam	24	4.5 (-5.8, 14.7)	0.393	23	-0.4 (-12.7, 12.0)	0.951
	Other Polytherapy	27	-3.2 (-12.3, 5.9)	0.494	27	-2.9 (-12.0, 6.2)	0.529
Age 4.5	Lamotrigine	79	7.4 (-1.9, 16.8)	0.117	77	7.4 (-1.6, 16.4)	0.107
	Levetiracetam	71	12.3 (4.0, 20.5)	0.004	64	13.4 (4.9, 21.8)	0.002
	Other Monotherapy	33	-1.5 (-20.7, 17.7)	0.878	30	-0.7 (-16.7, 15.4)	0.933
	Lamotrigine+ Levetiracetam	24	4.4 (-5.8, 14.7)	0.396	22	-0.7 (-12.3, 10.8)	0.902
	Other Polytherapy	25	0.2 (-13.8, 14.2)	0.982	25	0.5 (-15.5, 16.5)	0.954
<i>P-Value for Interaction Term^e</i>		-	-	0.318	-	-	0.330

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
BASC-2 Aggression Subscale T-Score							
Age 2	Lamotrigine	96	9.8 (3.0, 16.7)	0.005	94	9.6 (2.8, 16.4)	0.006
	Levetiracetam	71	-1.5 (-5.1, 2.0)	0.397	68	-1.5 (-5.2, 2.2)	0.420
	Other Monotherapy	44	5.0 (-9.6, 19.5)	0.503	41	6.3 (-6.6, 19.3)	0.337
	Lamotrigine+ Levetiracetam	27	-0.1 (-6.8, 6.5)	0.974	26	-0.1 (-8.5, 8.2)	0.976
	Other Polytherapy	27	-4.2 (-10.7, 2.3)	0.210	27	-4.3 (-10.7, 2.0)	0.182
Age 3	Lamotrigine	94	8.0 (1.1, 14.9)	0.023	89	7.7 (0.3, 15.1)	0.040
	Levetiracetam	74	4.8 (0.5, 9.1)	0.029	68	5.2 (0.9, 9.4)	0.017
	Other Monotherapy	41	4.9 (-13.9, 23.8)	0.608	38	6.9 (-11.0, 24.9)	0.449
	Lamotrigine+ Levetiracetam	24	4.5 (-1.8, 10.8)	0.161	23	3.7 (-4.1, 11.4)	0.353
	Other Polytherapy	27	-2.9 (-10.4, 4.6)	0.452	27	-3.0 (-9.7, 3.7)	0.378
Age 4.5	Lamotrigine	79	4.2 (-2.0, 10.5)	0.183	77	3.4 (-2.5, 9.3)	0.258
	Levetiracetam	71	6.6 (-0.3, 13.4)	0.059	64	7.3 (0.1, 14.5)	0.048
	Other Monotherapy	33	4.9 (-11.0, 20.8)	0.548	30	5.8 (-8.1, 19.8)	0.414
	Lamotrigine+ Levetiracetam	24	-4.2 (-11.2, 2.7)	0.231	22	-4.8 (-13.7, 4.0)	0.285
	Other Polytherapy	25	2.6 (-4.8, 10.0)	0.489	25	2.4 (-6.0, 10.9)	0.571
<i>P-Value for Interaction Term^e</i>		-	-	0.069	-	-	0.062
BASC-2 Anxiety Subscale T-Score							
Age 2	Lamotrigine	94	-2.9 (-9.5, 3.7)	0.391	92	-2.0 (-8.9, 4.9)	0.572
	Levetiracetam	71	-7.2 (-12.4, -2.0)	0.006	68	-7.4 (-12.6, -2.1)	0.006
	Other Monotherapy	44	-0.3 (-10.9, 10.4)	0.960	41	2.6 (-6.6, 11.8)	0.578
	Lamotrigine+ Levetiracetam	27	1.8 (-8.2, 11.8)	0.729	26	-0.8 (-11.4, 9.7)	0.878

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Polytherapy	27	-5.9 (-12.6, 0.7)	0.080	27	-4.3 (-10.9, 2.3)	0.204
Age 3	Lamotrigine	94	-0.9 (-11.3, 9.5)	0.867	89	0.2 (-10.6, 11.0)	0.972
	Levetiracetam	73	-4.7 (-11.5, 2.1)	0.172	67	-4.7 (-11.8, 2.3)	0.189
	Other Monotherapy	41	4.3 (-8.5, 17.2)	0.510	38	8.3 (-3.5, 20.1)	0.170
	Lamotrigine+ Levetiracetam	24	3.1 (-8.0, 14.1)	0.587	23	-0.4 (-10.8, 10.0)	0.935
	Other Polytherapy	27	1.9 (-9.7, 13.4)	0.748	27	3.6 (-7.2, 14.4)	0.514
Age 4.5	Lamotrigine	79	-2.4 (-12.3, 7.6)	0.641	77	-1.7 (-11.7, 8.2)	0.732
	Levetiracetam	71	-1.9 (-8.8, 5.1)	0.600	64	-1.7 (-9.2, 5.7)	0.651
	Other Monotherapy	33	0.2 (-17.7, 18.1)	0.984	30	4.7 (-10.4, 19.8)	0.542
	Lamotrigine+ Levetiracetam	24	4.7 (-2.0, 11.3)	0.167	22	3.1 (-5.2, 11.4)	0.465
	Other Polytherapy	25	9.5 (1.1, 17.9)	0.026	25	11.2 (3.3, 19.1)	0.006
<i>P-Value for Interaction Term^e</i>		-	-	0.644	-	-	0.629
BASC-2 Depression Subscale T-Score							
Age 2	Lamotrigine	96	6.0 (-3.6, 15.6)	0.219	94	6.2 (-2.5, 14.9)	0.162
	Levetiracetam	71	-1.7 (-6.9, 3.6)	0.536	68	-1.9 (-7.7, 3.8)	0.505
	Other Monotherapy	44	5.4 (-10.4, 21.2)	0.504	41	5.8 (-8.1, 19.7)	0.414
	Lamotrigine+ Levetiracetam	27	1.5 (-4.3, 7.3)	0.614	26	0.6 (-6.8, 8.0)	0.871
	Other Polytherapy	27	-1.7 (-9.2, 5.7)	0.648	27	-2.1 (-10.1, 5.8)	0.600
Age 3	Lamotrigine	94	3.3 (-6.6, 13.2)	0.512	89	3.5 (-6.2, 13.3)	0.475
	Levetiracetam	74	0.9 (-6.5, 8.2)	0.820	68	0.8 (-6.6, 8.3)	0.825
	Other Monotherapy	41	3.8 (-14.5, 22.1)	0.684	38	5.6 (-11.0, 22.2)	0.512
	Lamotrigine+ Levetiracetam	24	5.2 (-1.9, 12.3)	0.152	23	3.3 (-5.5, 12.1)	0.463

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Polytherapy	27	-5.5 (-13.4, 2.4)	0.172	27	-5.8 (-13.3, 1.6)	0.125
Age 4.5	Lamotrigine	79	8.6 (-1.6, 18.8)	0.097	77	8.4 (-1.1, 17.9)	0.084
	Levetiracetam	71	3.2 (-3.9, 10.3)	0.375	64	3.4 (-3.8, 10.6)	0.353
	Other Monotherapy	33	3.5 (-23.9, 30.9)	0.803	30	5.2 (-19.4, 29.8)	0.680
	Lamotrigine+ Levetiracetam	24	4.9 (-4.1, 13.8)	0.285	22	2.6 (-9.5, 14.7)	0.672
	Other Polytherapy	25	-4.5 (-22.8, 13.8)	0.632	25	-4.8 (-24.1, 14.4)	0.623
<i>P-Value for Interaction Term^e</i>		-	-	0.857	-	-	0.927
BASC-2 Somatization Subscale T-Score							
Age 2	Lamotrigine	96	0.3 (-6.6, 7.2)	0.923	94	-0.1 (-7.5, 7.2)	0.971
	Levetiracetam	71	11.1 (7.1, 15.1)	<.001	68	11.2 (7.5, 15.0)	<.001
	Other Monotherapy	44	-5.1 (-16.8, 6.6)	0.390	41	-5.7 (-18.3, 6.9)	0.372
	Lamotrigine+ Levetiracetam	27	-1.0 (-8.8, 6.9)	0.809	26	-6.6 (-13.8, 0.6)	0.071
	Other Polytherapy	27	-9.9 (-21.3, 1.6)	0.090	27	-10.7 (-21.5, 0.1)	0.052
Age 3	Lamotrigine	94	-2.1 (-10.5, 6.4)	0.633	89	-3.0 (-12.2, 6.2)	0.519
	Levetiracetam	74	8.3 (3.1, 13.5)	0.002	68	8.3 (3.2, 13.4)	0.001
	Other Monotherapy	41	-7.6 (-21.7, 6.4)	0.287	38	-7.8 (-22.3, 6.6)	0.288
	Lamotrigine+ Levetiracetam	24	1.4 (-9.2, 12.0)	0.793	23	-6.7 (-15.3, 2.0)	0.130
	Other Polytherapy	27	-6.2 (-16.1, 3.6)	0.215	27	-7.1 (-17.4, 3.2)	0.175
Age 4.5	Lamotrigine	79	1.5 (-7.8, 10.8)	0.751	77	0.5 (-8.9, 10.0)	0.916
	Levetiracetam	71	5.9 (-0.7, 12.5)	0.078	64	6.0 (-0.9, 12.9)	0.088
	Other Monotherapy	33	-2.4 (-13.0, 8.2)	0.658	30	-2.3 (-13.4, 8.8)	0.686
	Lamotrigine+ Levetiracetam	24	0.6 (-10.6, 11.8)	0.918	22	-8.7 (-15.8, -1.6)	0.016

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Polytherapy	25	-8.7 (-16.7, -0.8)	0.032	25	-9.6 (-18.1, -1.0)	0.028
<i>P-Value for Interaction Term^e</i>		-	-	0.821	-	-	0.895
BASC-2 Atypicality Subscale T-Score							
Age 2	Lamotrigine	96	6.8 (-0.3, 13.8)	0.062	94	7.2 (0.3, 14.0)	0.040
	Levetiracetam	70	-2.0 (-9.0, 4.9)	0.566	67	-1.7 (-8.8, 5.5)	0.649
	Other Monotherapy	44	-2.0 (-17.1, 13.1)	0.798	41	-2.7 (-17.2, 11.8)	0.718
	Lamotrigine+ Levetiracetam	27	9.6 (5.2, 14.0)	<.001	26	6.7 (2.2, 11.3)	0.004
	Other Polytherapy	27	-1.5 (-11.2, 8.1)	0.758	27	-1.0 (-9.7, 7.6)	0.817
Age 3	Lamotrigine	94	5.9 (-2.2, 14.0)	0.156	89	6.7 (-2.1, 15.6)	0.137
	Levetiracetam	74	3.7 (-2.7, 10.1)	0.259	68	4.7 (-1.8, 11.3)	0.156
	Other Monotherapy	41	0.7 (-20.4, 21.8)	0.945	38	0.1 (-18.8, 18.9)	0.995
	Lamotrigine+ Levetiracetam	24	4.4 (-3.5, 12.3)	0.275	23	0.6 (-8.3, 9.5)	0.896
	Other Polytherapy	27	-0.8 (-7.4, 5.9)	0.821	27	-0.2 (-6.3, 5.8)	0.941
Age 4.5	Lamotrigine	79	4.0 (-3.8, 11.8)	0.315	77	3.9 (-3.5, 11.4)	0.301
	Levetiracetam	71	8.7 (2.4, 15.0)	0.007	64	9.0 (2.1, 15.8)	0.011
	Other Monotherapy	33	-1.5 (-24.0, 21.0)	0.895	30	-2.6 (-22.3, 17.0)	0.794
	Lamotrigine+ Levetiracetam	24	6.3 (-2.0, 14.7)	0.139	22	0.3 (-8.2, 8.8)	0.941
	Other Polytherapy	25	-0.5 (-15.6, 14.6)	0.947	25	0.0 (-16.7, 16.7)	0.997
<i>P-Value for Interaction Term^e</i>		-	-	0.475	-	-	0.381
BASC-2 Withdrawal Subscale T-Score							
Age 2	Lamotrigine	96	-1.5 (-9.8, 6.8)	0.728	94	-0.3 (-8.6, 8.1)	0.949
	Levetiracetam	70	-4.2 (-9.6, 1.1)	0.122	67	-3.1 (-8.5, 2.3)	0.264

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Monotherapy	44	-7.5 (-14.9, -0.2)	0.043	41	-6.6 (-14.9, 1.6)	0.113
	Lamotrigine+ Levetiracetam	27	0.5 (-6.4, 7.4)	0.888	26	0.7 (-7.4, 8.8)	0.865
	Other Polytherapy	27	4.2 (-4.1, 12.6)	0.323	27	2.8 (-5.8, 11.5)	0.517
Age 3	Lamotrigine	94	-3.0 (-9.6, 3.6)	0.374	89	-1.4 (-8.1, 5.3)	0.673
	Levetiracetam	73	-0.2 (-7.1, 6.8)	0.966	67	0.3 (-7.2, 7.8)	0.933
	Other Monotherapy	41	10.1 (-2.4, 22.6)	0.113	38	11.5 (0.6, 22.3)	0.039
	Lamotrigine+ Levetiracetam	24	1.8 (-5.3, 8.8)	0.626	23	2.3 (-6.5, 11.2)	0.602
	Other Polytherapy	27	4.0 (-4.7, 12.7)	0.367	27	2.6 (-5.9, 11.2)	0.546
Age 4.5	Lamotrigine	79	-2.4 (-10.6, 5.8)	0.564	77	-1.5 (-10.0, 7.1)	0.737
	Levetiracetam	71	4.1 (-5.3, 13.5)	0.392	64	4.9 (-5.0, 14.7)	0.332
	Other Monotherapy	33	1.2 (-14.5, 16.8)	0.885	30	2.9 (-10.7, 16.4)	0.678
	Lamotrigine+ Levetiracetam	24	-0.9 (-6.2, 4.4)	0.729	22	0.1 (-7.3, 7.4)	0.988
	Other Polytherapy	25	6.4 (-4.5, 17.3)	0.252	25	5.0 (-5.8, 15.7)	0.366
<i>P-Value for Interaction Term^e</i>		-	-	0.354	-	-	0.409
BASC-2 Attention Problems Subscale T-Score							
Age 2	Lamotrigine	96	-2.6 (-9.8, 4.7)	0.490	94	-1.8 (-9.1, 5.5)	0.628
	Levetiracetam	71	4.6 (-1.9, 11.0)	0.166	68	5.7 (-0.7, 12.2)	0.081
	Other Monotherapy	44	7.1 (-2.9, 17.1)	0.165	41	5.1 (-4.8, 14.9)	0.313
	Lamotrigine+ Levetiracetam	27	5.9 (-0.3, 12.2)	0.063	26	3.7 (-2.3, 9.8)	0.228
	Other Polytherapy	27	-6.0 (-15.5, 3.5)	0.219	27	-6.5 (-16.7, 3.7)	0.212
Age 3	Lamotrigine	94	-3.8 (-12.2, 4.7)	0.380	89	-2.1 (-10.3, 6.0)	0.610
	Levetiracetam	74	5.7 (-1.5, 13.0)	0.118	68	7.8 (0.6, 15.0)	0.034

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Monotherapy	41	2.0 (-16.0, 20.1)	0.826	38	1.6 (-16.9, 20.1)	0.865
	Lamotrigine+ Levetiracetam	24	1.8 (-8.4, 11.9)	0.735	23	-2.1 (-12.4, 8.1)	0.682
	Other Polytherapy	27	-5.0 (-13.0, 3.1)	0.227	27	-5.5 (-14.2, 3.3)	0.221
Age 4.5	Lamotrigine	79	-0.4 (-8.6, 7.8)	0.933	77	1.1 (-6.6, 8.8)	0.778
	Levetiracetam	71	8.1 (2.0, 14.2)	0.009	64	10.5 (4.7, 16.4)	<.001
	Other Monotherapy	33	-4.9 (-18.9, 9.2)	0.499	30	-6.4 (-19.6, 6.8)	0.343
	Lamotrigine+ Levetiracetam	24	3.2 (-5.4, 11.8)	0.465	22	-1.9 (-10.0, 6.1)	0.641
	Other Polytherapy	25	-1.6 (-14.6, 11.5)	0.812	25	-2.2 (-16.4, 11.9)	0.758
<i>P-Value for Interaction Term^e</i>		-	-	0.599	-	-	0.396
BASC-2 Adaptability Subscale T-Score							
Age 2	Lamotrigine	96	-2.4 (-10.3, 5.6)	0.564	94	-3.7 (-11.6, 4.2)	0.358
	Levetiracetam	71	3.9 (-2.4, 10.2)	0.228	68	3.2 (-2.9, 9.3)	0.305
	Other Monotherapy	44	-9.0 (-19.1, 1.2)	0.083	41	-8.8 (-19.3, 1.6)	0.098
	Lamotrigine+ Levetiracetam	27	0.7 (-10.0, 11.5)	0.896	26	3.2 (-7.0, 13.4)	0.542
	Other Polytherapy	27	-1.3 (-10.0, 7.3)	0.763	27	0.1 (-9.1, 9.3)	0.981
Age 3	Lamotrigine	94	-2.3 (-10.8, 6.3)	0.605	89	-4.0 (-11.8, 3.8)	0.318
	Levetiracetam	74	-1.1 (-9.8, 7.5)	0.801	68	-1.2 (-9.6, 7.2)	0.781
	Other Monotherapy	41	-15.4 (-29.9, -1.0)	0.036	38	-14.3 (-27.0, -1.6)	0.027
	Lamotrigine+ Levetiracetam	24	-10.2 (-21.0, 0.5)	0.062	23	-7.3 (-18.3, 3.7)	0.194
	Other Polytherapy	27	0.3 (-7.8, 8.3)	0.949	27	1.7 (-7.5, 10.8)	0.718
Age 4.5	Lamotrigine	79	-2.5 (-12.6, 7.7)	0.635	77	-4.4 (-14.7, 5.9)	0.402
	Levetiracetam	71	-7.9 (-17.8, 1.9)	0.116	64	-9.3 (-18.7, 0.2)	0.055

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Monotherapy	33	-0.6 (-18.2, 17.1)	0.949	30	0.9 (-14.6, 16.4)	0.908
	Lamotrigine+ Levetiracetam	24	0.1 (-9.6, 9.8)	0.978	22	4.1 (-5.0, 13.2)	0.376
	Other Polytherapy	25	-0.5 (-12.4, 11.5)	0.940	25	1.1 (-11.1, 13.3)	0.855
<i>P-Value for Interaction Term^e</i>		-	-	0.056	-	-	0.023
BASC-2 Social Skills Subscale T-Score							
Age 2	Lamotrigine	96	-0.4 (-7.4, 6.6)	0.914	94	-1.3 (-8.3, 5.7)	0.719
	Levetiracetam	71	-7.9 (-12.6, -3.1)	0.001	68	-8.6 (-13.5, -3.8)	<.001
	Other Monotherapy	44	-2.9 (-13.1, 7.3)	0.576	41	0.3 (-9.4, 10.1)	0.949
	Lamotrigine+ Levetiracetam	27	1.4 (-10.6, 13.5)	0.814	26	0.7 (-12.4, 13.7)	0.922
	Other Polytherapy	27	-4.3 (-12.8, 4.2)	0.318	27	-3.7 (-12.2, 4.9)	0.397
Age 3	Lamotrigine	94	-2.5 (-9.8, 4.9)	0.507	89	-4.8 (-11.6, 1.9)	0.160
	Levetiracetam	74	-6.2 (-12.4, 0.0)	0.050	68	-7.1 (-13.3, -0.8)	0.026
	Other Monotherapy	41	-8.7 (-22.7, 5.2)	0.218	38	-6.4 (-18.8, 6.1)	0.317
	Lamotrigine+ Levetiracetam	24	1.9 (-7.4, 11.1)	0.690	23	0.9 (-10.2, 12.0)	0.874
	Other Polytherapy	27	-1.1 (-13.5, 11.4)	0.868	27	-0.4 (-14.1, 13.2)	0.949
Age 4.5	Lamotrigine	79	-2.4 (-11.8, 7.0)	0.617	77	-4.4 (-13.5, 4.7)	0.344
	Levetiracetam	71	-10.1 (-18.4, -1.9)	0.016	64	-11.7 (-19.8, -3.5)	0.005
	Other Monotherapy	33	7.2 (-8.1, 22.6)	0.357	30	11.6 (-2.2, 25.5)	0.100
	Lamotrigine+ Levetiracetam	24	1.0 (-6.6, 8.6)	0.793	22	-0.4 (-9.3, 8.6)	0.937
	Other Polytherapy	25	-1.5 (-17.7, 14.7)	0.857	25	-0.8 (-17.9, 16.3)	0.923
<i>P-Value for Interaction Term^e</i>		-	-	0.833	-	-	0.672

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value

N = children of WWE with non-missing behavior score and mothers with max observed ratio ASM Concentration in 3rd

trimester (includes day of delivery). Children with missing covariates excluded from adjusted model.

^a Ratio ASM Concentration calculated as ratio upper limit for therapeutic range. For mothers on polytherapy, ratio ASM concentration calculated by summing the ratio ASM concentration for each ASM. Maximum observed value recorded during 3rd trimester, including day of delivery.

^b Parameter Estimate and P-Value from a longitudinal generalized linear model with identity link function and generalized estimating equations and unstructured covariance structure including mother's max observed ratio ASM

concentration in 3rd trimester, ASM category, child's age, their interaction, and all lower order interactions.

^c Adjusted for mother's IQ, education level, age at enrollment, smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status. Mother's ASM group was not included as a covariate in model.

^d Based on ASM regimen taken at time of blood draw for maximum observed ratio ASM concentration during 3rd trimester (includes day of delivery).

^e P-value for the interaction between max observed ratio ASM concentration in 3rd trimester, ASM category, and child's age calculated using the Score test. If significant, the association between max observed ratio ASM concentration in 3rd trimester and behavior score differs among child's age and ASM category.

eTable 23. Association Between Continuous Behavior Scores and Maximum Ratio DDD^a in 3rd Trimester by ASM Category and Child's Age, Children of WWE With 3rd Trimester Blood Levels, Completers Population

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
ABAS-3 General Adaptive Composite Standard Score							
Age 3	Lamotrigine	93	-2.2 (-4.5, 0.1)	0.065	88	-2.3 (-4.3, -0.2)	0.031
	Levetiracetam	76	-1.4 (-4.8, 1.9)	0.406	68	-2.1 (-5.1, 1.0)	0.189
	Other Monotherapy	46	1.6 (-3.7, 6.9)	0.551	43	3.8 (-1.8, 9.5)	0.181
	Lamotrigine+ Levetiracetam	26	-1.9 (-5.8, 2.0)	0.333	25	-0.9 (-3.9, 2.1)	0.565
	Other Polytherapy	37	-2.0 (-3.5, -0.6)	0.006	36	-1.5 (-3.0, 0.1)	0.059
Age 4.5	Lamotrigine	78	-2.4 (-4.7, -0.1)	0.045	76	-2.4 (-4.6, -0.3)	0.028
	Levetiracetam	71	-5.4 (-8.8, -2.0)	0.002	63	-6.5 (-9.5, -3.5)	<.001
	Other Monotherapy	33	2.7 (-2.8, 8.2)	0.335	32	4.8 (0.3, 9.4)	0.038
	Lamotrigine+ Levetiracetam	24	-1.3 (-6.0, 3.3)	0.568	22	0.3 (-2.4, 2.9)	0.843
	Other Polytherapy	33	-1.9 (-3.0, -0.8)	<.001	33	-1.3 (-2.7, 0.1)	0.076
<i>P-Value for Interaction Term^e</i>		-	-	0.079	-	-	0.028
ABAS-3 Conceptual Composite Standard Score							
Age 3	Lamotrigine	93	-1.4 (-3.6, 0.9)	0.240	88	-1.5 (-3.6, 0.7)	0.176
	Levetiracetam	77	-3.3 (-8.0, 1.4)	0.166	69	-3.2 (-6.9, 0.6)	0.100
	Other Monotherapy	46	3.1 (-2.2, 8.4)	0.249	43	4.5 (-1.2, 10.1)	0.120
	Lamotrigine+ Levetiracetam	26	-1.4 (-6.2, 3.4)	0.575	25	-0.7 (-3.9, 2.6)	0.690
	Other Polytherapy	37	-2.4 (-4.0, -0.8)	0.003	36	-1.5 (-3.2, 0.2)	0.082
Age 4.5	Lamotrigine	78	-1.7 (-3.9, 0.5)	0.139	76	-1.7 (-3.8, 0.3)	0.097
	Levetiracetam	71	-4.9 (-9.2, -0.6)	0.026	63	-5.5 (-9.2, -1.7)	0.004
	Other Monotherapy	33	3.3 (-2.4, 9.1)	0.257	32	4.8 (-0.1, 9.6)	0.056

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Lamotrigine+ Levetiracetam	24	-0.8 (-5.2, 3.7)	0.735	22	0.4 (-2.0, 2.7)	0.771
	Other Polytherapy	33	-2.7 (-3.9, -1.4)	<.001	33	-1.7 (-3.1, -0.3)	0.016
<i>P-Value for Interaction Term^e</i>		-	-	0.795	-	-	0.457
ABAS-3 Social Composite Standard Score							
Age 3	Lamotrigine	93	-2.0 (-4.4, 0.4)	0.095	88	-2.0 (-4.0, 0.1)	0.059
	Levetiracetam	76	-1.5 (-4.5, 1.6)	0.341	68	-2.1 (-5.1, 0.9)	0.178
	Other Monotherapy	46	0.4 (-5.1, 5.9)	0.885	43	3.4 (-2.5, 9.3)	0.260
	Lamotrigine+ Levetiracetam	26	-1.3 (-4.7, 2.1)	0.443	25	-1.1 (-4.7, 2.5)	0.557
	Other Polytherapy	37	-2.6 (-4.2, -0.9)	0.002	36	-2.0 (-3.9, -0.1)	0.039
Age 4.5	Lamotrigine	80	-1.4 (-3.7, 0.9)	0.248	78	-1.3 (-3.5, 0.8)	0.228
	Levetiracetam	71	-4.8 (-8.0, -1.6)	0.003	63	-5.7 (-8.6, -2.9)	<.001
	Other Monotherapy	33	0.2 (-4.8, 5.3)	0.932	32	2.8 (-1.9, 7.4)	0.242
	Lamotrigine+ Levetiracetam	24	-0.1 (-4.5, 4.3)	0.964	22	0.5 (-2.2, 3.3)	0.697
	Other Polytherapy	34	-2.7 (-3.9, -1.5)	<.001	33	-2.2 (-3.5, -0.9)	0.001
<i>P-Value for Interaction Term^e</i>		-	-	0.192	-	-	0.114
ABAS-3 Practical Composite Standard Score							
Age 3	Lamotrigine	93	-2.2 (-4.6, 0.2)	0.078	88	-2.1 (-4.2, 0.1)	0.056
	Levetiracetam	77	-1.9 (-5.2, 1.5)	0.281	69	-2.2 (-5.2, 0.8)	0.145
	Other Monotherapy	46	1.5 (-3.7, 6.7)	0.575	43	4.2 (-1.4, 9.8)	0.142
	Lamotrigine+ Levetiracetam	26	-2.6 (-6.2, 1.1)	0.167	25	-2.0 (-5.3, 1.3)	0.229
	Other Polytherapy	37	-1.3 (-2.7, 0.2)	0.088	36	-0.9 (-2.2, 0.5)	0.207
Age 4.5	Lamotrigine	79	-2.7 (-5.2, -0.3)	0.029	77	-2.6 (-4.9, -0.3)	0.027

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Levetiracetam	71	-6.2 (-9.4, -3.0)	<.001	63	-6.9 (-9.7, -4.2)	<.001
	Other Monotherapy	33	4.0 (-1.1, 9.0)	0.123	32	6.4 (2.2, 10.6)	0.003
	Lamotrigine+ Levetiracetam	24	-1.5 (-5.4, 2.5)	0.467	22	-0.1 (-2.8, 2.7)	0.969
	Other Polytherapy	34	-0.4 (-1.9, 1.1)	0.623	33	0.0 (-1.9, 1.8)	0.961
<i>P-Value for Interaction Term^e</i>		-	-	0.021	-	-	0.006
BASC-2 Hyperactivity Subscale T-Score							
Age 2	Lamotrigine	96	0.9 (-0.7, 2.4)	0.272	94	0.9 (-0.7, 2.4)	0.260
	Levetiracetam	72	1.2 (-1.5, 3.9)	0.374	69	1.4 (-1.2, 3.9)	0.293
	Other Monotherapy	46	0.0 (-3.0, 3.0)	0.996	44	-0.3 (-3.5, 2.9)	0.870
	Lamotrigine+ Levetiracetam	29	2.2 (-1.8, 6.3)	0.277	28	0.2 (-3.1, 3.4)	0.911
	Other Polytherapy	39	1.7 (-0.3, 3.7)	0.088	37	1.3 (-0.6, 3.2)	0.170
Age 3	Lamotrigine	94	1.5 (-0.4, 3.3)	0.130	89	1.5 (-0.5, 3.4)	0.137
	Levetiracetam	75	0.4 (-1.6, 2.4)	0.684	68	0.6 (-1.3, 2.5)	0.521
	Other Monotherapy	45	0.1 (-3.2, 3.4)	0.934	42	-0.8 (-4.2, 2.6)	0.640
	Lamotrigine+ Levetiracetam	26	2.4 (0.1, 4.6)	0.041	25	1.2 (-1.6, 4.0)	0.402
	Other Polytherapy	37	1.6 (0.1, 3.1)	0.034	36	1.2 (-0.3, 2.7)	0.107
Age 4.5	Lamotrigine	78	1.5 (0.0, 3.0)	0.045	76	1.5 (-0.1, 3.0)	0.058
	Levetiracetam	72	3.7 (0.2, 7.1)	0.037	64	3.8 (0.2, 7.4)	0.040
	Other Monotherapy	34	0.6 (-3.5, 4.7)	0.787	32	0.1 (-4.5, 4.7)	0.969
	Lamotrigine+ Levetiracetam	24	1.2 (-2.2, 4.6)	0.494	22	-1.2 (-4.0, 1.6)	0.385
	Other Polytherapy	34	1.5 (-0.7, 3.8)	0.185	33	1.1 (-1.1, 3.3)	0.342
<i>P-Value for Interaction Term^e</i>		-	-	0.775	-	-	0.636

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
BASC-2 Aggression Subscale T-Score							
Age 2	Lamotrigine	96	0.9 (-0.3, 2.1)	0.151	94	0.8 (-0.4, 2.1)	0.194
	Levetiracetam	72	0.2 (-0.9, 1.4)	0.700	69	0.3 (-0.9, 1.5)	0.633
	Other Monotherapy	46	-0.2 (-3.8, 3.3)	0.899	44	0.3 (-3.4, 4.0)	0.859
	Lamotrigine+ Levetiracetam	29	0.3 (-1.7, 2.4)	0.753	28	0.1 (-2.1, 2.3)	0.908
	Other Polytherapy	39	1.1 (-1.0, 3.1)	0.299	37	0.8 (-1.2, 2.8)	0.421
Age 3	Lamotrigine	94	0.9 (-0.5, 2.3)	0.224	89	0.8 (-0.7, 2.4)	0.283
	Levetiracetam	75	2.0 (0.5, 3.4)	0.007	68	2.0 (0.6, 3.4)	0.005
	Other Monotherapy	45	-1.4 (-3.9, 1.2)	0.287	42	-0.9 (-3.8, 1.9)	0.523
	Lamotrigine+ Levetiracetam	26	1.8 (-0.6, 4.2)	0.138	25	2.0 (-0.4, 4.4)	0.096
	Other Polytherapy	37	1.5 (-0.3, 3.4)	0.100	36	1.2 (-0.4, 2.9)	0.148
Age 4.5	Lamotrigine	78	0.0 (-1.3, 1.3)	0.967	76	-0.3 (-1.5, 1.0)	0.663
	Levetiracetam	72	1.8 (-0.4, 4.0)	0.102	64	2.0 (-0.3, 4.3)	0.095
	Other Monotherapy	34	-0.6 (-3.5, 2.3)	0.682	32	-0.6 (-3.6, 2.3)	0.675
	Lamotrigine+ Levetiracetam	24	0.8 (-1.3, 2.9)	0.459	22	0.2 (-2.1, 2.4)	0.881
	Other Polytherapy	34	0.3 (-0.8, 1.4)	0.619	33	-0.1 (-1.2, 1.1)	0.920
<i>P-Value for Interaction Term^e</i>		-	-	0.381	-	-	0.337
BASC-2 Anxiety Subscale T-Score							
Age 2	Lamotrigine	94	-0.6 (-1.9, 0.6)	0.329	92	-0.8 (-2.1, 0.5)	0.254
	Levetiracetam	72	-1.1 (-3.2, 1.0)	0.322	69	-1.3 (-3.3, 0.8)	0.233
	Other Monotherapy	46	0.8 (-2.1, 3.6)	0.604	44	0.1 (-2.3, 2.6)	0.921
	Lamotrigine+ Levetiracetam	29	0.7 (-2.8, 4.2)	0.702	28	1.9 (-1.2, 4.9)	0.231

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Polytherapy	39	0.2 (-0.9, 1.4)	0.686	37	-0.1 (-1.4, 1.2)	0.895
Age 3	Lamotrigine	94	-0.7 (-2.4, 0.9)	0.370	89	-0.9 (-2.5, 0.7)	0.269
	Levetiracetam	74	-1.0 (-3.3, 1.4)	0.424	67	-1.3 (-3.6, 1.0)	0.271
	Other Monotherapy	45	0.1 (-3.9, 4.1)	0.952	42	-1.4 (-4.6, 1.8)	0.401
	Lamotrigine+ Levetiracetam	26	3.2 (-0.4, 6.7)	0.079	25	4.8 (2.6, 7.0)	<.001
	Other Polytherapy	37	0.2 (-1.2, 1.6)	0.812	36	-0.2 (-1.7, 1.3)	0.817
Age 4.5	Lamotrigine	78	0.3 (-1.5, 2.2)	0.717	76	0.2 (-1.7, 2.2)	0.811
	Levetiracetam	72	-0.1 (-2.8, 2.7)	0.965	64	-0.1 (-3.0, 2.8)	0.951
	Other Monotherapy	34	2.1 (-2.6, 6.9)	0.374	32	3.0 (-1.5, 7.4)	0.189
	Lamotrigine+ Levetiracetam	24	3.6 (1.8, 5.4)	<.001	22	3.7 (1.6, 5.8)	<.001
	Other Polytherapy	34	-1.4 (-2.7, -0.1)	0.041	33	-1.6 (-3.2, -0.1)	0.035
<i>P-Value for Interaction Term^e</i>		-	-	0.518	-	-	0.271
BASC-2 Depression Subscale T-Score							
Age 2	Lamotrigine	96	1.3 (0.2, 2.4)	0.020	94	1.3 (0.2, 2.4)	0.026
	Levetiracetam	72	0.2 (-1.3, 1.6)	0.834	69	0.1 (-1.4, 1.6)	0.868
	Other Monotherapy	46	1.4 (-1.7, 4.5)	0.380	44	0.2 (-3.1, 3.4)	0.919
	Lamotrigine+ Levetiracetam	29	2.3 (-0.9, 5.4)	0.155	28	0.9 (-2.0, 3.9)	0.545
	Other Polytherapy	39	0.8 (-1.3, 2.8)	0.463	37	0.5 (-1.5, 2.5)	0.606
Age 3	Lamotrigine	94	0.8 (-0.9, 2.6)	0.352	89	0.7 (-1.1, 2.5)	0.418
	Levetiracetam	75	0.3 (-1.9, 2.5)	0.781	68	0.3 (-1.9, 2.5)	0.798
	Other Monotherapy	45	0.7 (-2.7, 4.1)	0.680	42	-1.1 (-4.3, 2.0)	0.471
	Lamotrigine+ Levetiracetam	26	4.3 (1.8, 6.8)	<.001	25	3.6 (0.8, 6.3)	0.011

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Polytherapy	37	1.0 (-0.6, 2.6)	0.234	36	0.7 (-0.8, 2.2)	0.366
Age 4.5	Lamotrigine	78	1.8 (0.1, 3.4)	0.041	76	1.6 (0.0, 3.3)	0.052
	Levetiracetam	72	0.9 (-1.5, 3.3)	0.468	64	1.0 (-1.4, 3.5)	0.408
	Other Monotherapy	34	0.2 (-4.8, 5.2)	0.932	32	-0.3 (-5.6, 4.9)	0.897
	Lamotrigine+ Levetiracetam	24	2.7 (0.3, 5.2)	0.028	22	1.4 (-1.0, 3.9)	0.248
	Other Polytherapy	34	0.0 (-1.5, 1.6)	0.961	33	-0.1 (-1.8, 1.6)	0.868
<i>P-Value for Interaction Term^e</i>		-	-	0.822	-	-	0.680
BASC-2 Somatization Subscale T-Score							
Age 2	Lamotrigine	96	0.6 (-0.8, 2.0)	0.395	94	0.3 (-1.2, 1.8)	0.665
	Levetiracetam	72	2.9 (1.6, 4.3)	<.001	69	2.8 (1.5, 4.1)	<.001
	Other Monotherapy	46	-1.9 (-5.3, 1.5)	0.275	44	-3.5 (-6.9, -0.2)	0.040
	Lamotrigine+ Levetiracetam	29	0.8 (-1.0, 2.6)	0.375	28	0.9 (-0.9, 2.6)	0.321
	Other Polytherapy	39	0.2 (-0.5, 0.8)	0.642	37	-0.1 (-0.8, 0.6)	0.773
Age 3	Lamotrigine	94	-0.6 (-2.2, 0.9)	0.421	89	-1.1 (-2.7, 0.6)	0.215
	Levetiracetam	75	2.4 (0.6, 4.3)	0.010	68	2.2 (0.4, 4.0)	0.019
	Other Monotherapy	45	-1.0 (-3.3, 1.3)	0.396	42	-2.5 (-5.1, 0.1)	0.063
	Lamotrigine+ Levetiracetam	26	-1.2 (-4.2, 1.8)	0.441	25	-0.3 (-2.7, 2.0)	0.774
	Other Polytherapy	37	0.5 (-0.5, 1.5)	0.362	36	0.2 (-0.9, 1.3)	0.764
Age 4.5	Lamotrigine	78	-0.6 (-2.4, 1.3)	0.556	76	-1.0 (-2.9, 0.9)	0.293
	Levetiracetam	72	1.5 (-0.7, 3.7)	0.178	64	1.2 (-1.1, 3.4)	0.308
	Other Monotherapy	34	-3.1 (-6.0, -0.2)	0.037	32	-3.8 (-6.4, -1.1)	0.006
	Lamotrigine+ Levetiracetam	24	0.4 (-2.4, 3.1)	0.797	22	0.2 (-1.9, 2.4)	0.822

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Polytherapy	34	-1.4 (-2.7, -0.2)	0.028	33	-1.6 (-3.0, -0.2)	0.024
<i>P-Value for Interaction Term^e</i>		-	-	0.697	-	-	0.819
BASC-2 Atypicality Subscale T-Score							
Age 2	Lamotrigine	96	1.1 (-0.6, 2.7)	0.202	94	1.1 (-0.6, 2.7)	0.209
	Levetiracetam	71	-0.3 (-2.6, 2.1)	0.816	68	-0.2 (-2.5, 2.2)	0.882
	Other Monotherapy	46	-1.5 (-4.4, 1.5)	0.326	44	-2.4 (-5.9, 1.2)	0.191
	Lamotrigine+ Levetiracetam	29	2.4 (-0.2, 5.0)	0.072	28	1.2 (-1.2, 3.6)	0.335
	Other Polytherapy	39	1.7 (0.7, 2.7)	<.001	37	1.6 (0.5, 2.7)	0.005
Age 3	Lamotrigine	94	0.3 (-1.2, 1.7)	0.737	89	0.2 (-1.3, 1.8)	0.774
	Levetiracetam	75	1.2 (-1.0, 3.3)	0.283	68	1.3 (-0.9, 3.5)	0.247
	Other Monotherapy	45	-0.9 (-4.7, 2.8)	0.633	42	-1.8 (-6.5, 2.9)	0.450
	Lamotrigine+ Levetiracetam	26	2.7 (0.4, 5.0)	0.021	25	1.4 (-0.3, 3.1)	0.118
	Other Polytherapy	37	0.6 (-0.6, 1.8)	0.331	36	0.3 (-1.0, 1.6)	0.649
Age 4.5	Lamotrigine	78	0.5 (-0.9, 1.9)	0.486	76	0.4 (-1.0, 1.8)	0.594
	Levetiracetam	72	3.2 (0.4, 5.9)	0.023	64	3.6 (0.7, 6.4)	0.014
	Other Monotherapy	34	-0.4 (-4.5, 3.7)	0.842	32	-1.4 (-5.5, 2.8)	0.521
	Lamotrigine+ Levetiracetam	24	1.1 (-1.5, 3.7)	0.406	22	-0.6 (-1.9, 0.8)	0.392
	Other Polytherapy	34	0.0 (-1.2, 1.3)	0.952	33	-0.2 (-1.7, 1.2)	0.769
<i>P-Value for Interaction Term^e</i>		-	-	0.221	-	-	0.171
BASC-2 Withdrawal Subscale T-Score							
Age 2	Lamotrigine	96	0.3 (-1.1, 1.8)	0.641	94	0.5 (-1.0, 2.0)	0.494
	Levetiracetam	71	-0.9 (-2.8, 1.0)	0.359	68	-0.4 (-2.2, 1.4)	0.673

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Monotherapy	46	-2.0 (-4.2, 0.2)	0.072	44	-2.9 (-5.7, -0.1)	0.039
	Lamotrigine+ Levetiracetam	29	1.9 (-0.4, 4.2)	0.108	28	1.4 (-1.0, 3.8)	0.242
	Other Polytherapy	39	-0.8 (-2.0, 0.4)	0.171	37	-1.2 (-2.4, -0.1)	0.039
Age 3	Lamotrigine	94	0.1 (-1.1, 1.2)	0.919	89	0.3 (-0.9, 1.5)	0.656
	Levetiracetam	74	0.0 (-2.4, 2.4)	0.982	67	0.4 (-2.1, 2.9)	0.728
	Other Monotherapy	45	1.6 (-1.7, 4.9)	0.338	42	0.5 (-3.6, 4.5)	0.815
	Lamotrigine+ Levetiracetam	26	2.4 (0.9, 4.0)	0.002	25	2.4 (0.4, 4.4)	0.017
	Other Polytherapy	37	1.2 (-1.0, 3.3)	0.291	36	0.8 (-1.3, 2.8)	0.455
Age 4.5	Lamotrigine	78	0.4 (-1.3, 2.1)	0.674	76	0.4 (-1.3, 2.1)	0.669
	Levetiracetam	72	1.1 (-1.7, 3.9)	0.444	64	1.5 (-1.5, 4.5)	0.320
	Other Monotherapy	34	1.1 (-2.9, 5.2)	0.578	32	0.7 (-3.9, 5.3)	0.771
	Lamotrigine+ Levetiracetam	24	0.6 (-1.1, 2.2)	0.491	22	0.3 (-1.5, 2.2)	0.729
	Other Polytherapy	34	1.1 (-0.2, 2.5)	0.102	33	0.7 (-0.6, 2.0)	0.291
<i>P-Value for Interaction Term^e</i>		-	-	0.268	-	-	0.371
BASC-2 Attention Problems Subscale T-Score							
Age 2	Lamotrigine	96	-0.2 (-1.5, 1.2)	0.812	94	0.0 (-1.5, 1.5)	0.969
	Levetiracetam	72	2.2 (-0.2, 4.6)	0.073	69	2.5 (0.1, 4.9)	0.039
	Other Monotherapy	46	1.0 (-2.4, 4.4)	0.565	44	-0.1 (-3.5, 3.3)	0.948
	Lamotrigine+ Levetiracetam	29	0.9 (-2.5, 4.2)	0.609	28	-1.3 (-3.8, 1.2)	0.318
	Other Polytherapy	39	0.7 (-0.8, 2.3)	0.342	37	0.6 (-1.1, 2.4)	0.466
Age 3	Lamotrigine	94	0.0 (-1.7, 1.6)	0.990	89	0.1 (-1.5, 1.8)	0.870
	Levetiracetam	75	3.1 (0.5, 5.6)	0.017	68	3.5 (1.0, 6.0)	0.006

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Monotherapy	45	-0.8 (-4.8, 3.1)	0.683	42	-3.0 (-7.1, 1.1)	0.157
	Lamotrigine+ Levetiracetam	26	0.9 (-2.5, 4.3)	0.595	25	-1.2 (-3.9, 1.6)	0.403
	Other Polytherapy	37	0.5 (-0.7, 1.7)	0.412	36	0.1 (-1.2, 1.3)	0.921
Age 4.5	Lamotrigine	78	0.2 (-1.3, 1.6)	0.840	76	0.2 (-1.3, 1.8)	0.752
	Levetiracetam	72	3.0 (0.5, 5.5)	0.018	64	3.6 (1.2, 6.0)	0.004
	Other Monotherapy	34	-0.7 (-3.7, 2.4)	0.675	32	-2.4 (-5.6, 0.8)	0.144
	Lamotrigine+ Levetiracetam	24	-0.3 (-3.5, 2.8)	0.830	22	-3.0 (-4.6, -1.5)	<.001
	Other Polytherapy	34	1.3 (-0.4, 2.9)	0.136	33	0.9 (-0.7, 2.5)	0.247
<i>P-Value for Interaction Term^e</i>		-	-	0.892	-	-	0.612
BASC-2 Adaptability Subscale T-Score							
Age 2	Lamotrigine	96	-0.8 (-2.1, 0.5)	0.225	94	-0.8 (-2.1, 0.5)	0.242
	Levetiracetam	72	-0.4 (-3.0, 2.3)	0.773	69	-0.5 (-3.0, 1.9)	0.665
	Other Monotherapy	46	-0.1 (-3.4, 3.2)	0.943	44	1.2 (-2.5, 4.8)	0.533
	Lamotrigine+ Levetiracetam	29	0.4 (-3.6, 4.4)	0.846	28	1.8 (-0.9, 4.6)	0.195
	Other Polytherapy	39	-0.3 (-1.7, 1.0)	0.636	37	0.3 (-1.1, 1.6)	0.711
Age 3	Lamotrigine	94	-0.6 (-2.1, 0.9)	0.460	89	-0.4 (-1.9, 1.1)	0.567
	Levetiracetam	75	-1.5 (-4.8, 1.7)	0.359	68	-1.8 (-4.7, 1.1)	0.226
	Other Monotherapy	45	-1.2 (-4.8, 2.5)	0.536	42	1.1 (-2.7, 4.9)	0.579
	Lamotrigine+ Levetiracetam	26	-0.9 (-4.8, 3.1)	0.669	25	0.3 (-2.9, 3.5)	0.843
	Other Polytherapy	37	-0.5 (-2.4, 1.3)	0.567	36	0.0 (-1.8, 1.8)	0.995
Age 4.5	Lamotrigine	78	-1.2 (-2.9, 0.5)	0.162	76	-1.2 (-2.9, 0.5)	0.169
	Levetiracetam	72	-2.8 (-6.5, 0.8)	0.129	64	-3.3 (-6.8, 0.2)	0.064

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value
	Other Monotherapy	34	0.8 (-3.1, 4.6)	0.697	32	2.5 (-1.4, 6.3)	0.209
	Lamotrigine+ Levetiracetam	24	0.9 (-3.5, 5.2)	0.692	22	2.6 (-0.4, 5.6)	0.093
	Other Polytherapy	34	0.2 (-1.0, 1.4)	0.689	33	0.7 (-0.4, 1.8)	0.207
<i>P-Value for Interaction Term^e</i>		-	-	0.534	-	-	0.520
BASC-2 Social Skills Subscale T-Score							
Age 2	Lamotrigine	96	-0.9 (-2.4, 0.7)	0.271	94	-1.1 (-2.7, 0.5)	0.191
	Levetiracetam	72	-2.1 (-3.7, -0.5)	0.011	69	-2.3 (-4.0, -0.6)	0.006
	Other Monotherapy	46	-0.1 (-3.1, 2.9)	0.940	44	1.3 (-1.7, 4.3)	0.406
	Lamotrigine+ Levetiracetam	29	-0.7 (-4.0, 2.6)	0.684	28	0.0 (-2.8, 2.7)	0.977
	Other Polytherapy	39	-0.4 (-1.4, 0.5)	0.360	37	-0.2 (-1.1, 0.7)	0.616
Age 3	Lamotrigine	94	-1.0 (-2.5, 0.6)	0.225	89	-1.3 (-2.9, 0.3)	0.124
	Levetiracetam	75	-2.2 (-4.4, 0.0)	0.053	68	-2.6 (-4.8, -0.4)	0.018
	Other Monotherapy	45	-0.6 (-4.0, 2.7)	0.709	42	1.0 (-2.9, 4.9)	0.613
	Lamotrigine+ Levetiracetam	26	-1.1 (-4.3, 2.1)	0.486	25	-0.6 (-3.5, 2.4)	0.701
	Other Polytherapy	37	-1.1 (-2.5, 0.4)	0.141	36	-0.8 (-2.3, 0.7)	0.288
Age 4.5	Lamotrigine	78	-0.4 (-2.3, 1.6)	0.729	76	-0.6 (-2.6, 1.5)	0.586
	Levetiracetam	72	-3.5 (-6.1, -0.8)	0.011	64	-3.8 (-6.6, -1.1)	0.007
	Other Monotherapy	34	2.3 (-1.4, 6.0)	0.222	32	4.1 (0.2, 8.0)	0.038
	Lamotrigine+ Levetiracetam	24	0.1 (-4.3, 4.5)	0.969	22	1.1 (-2.5, 4.6)	0.558
	Other Polytherapy	34	-1.6 (-3.5, 0.2)	0.088	33	-1.5 (-3.4, 0.3)	0.111
<i>P-Value for Interaction Term^e</i>		-	-	0.595	-	-	0.535

		Unadjusted ^b			Adjusted ^{bc}		
Child's Age	3rd Trimester ASM Category ^d	N	Parameter Estimate (95% CI)	P-Value	N	Parameter Estimate (95% CI)	P-Value

N = children of WWE on ASM in 3rd trimester with non-missing behavior score. Children with missing covariates excluded from adjusted model.

^a Ratio DDD = Ratio Defined Daily Dose, calculated by dividing the mother's ASM total prescribed daily dose by the WHO defined daily dose values. For mothers on polytherapy, ratio DDD equals the sum across the ratio DDD for all ASMs. Maximum ratio DDD during 3rd trimester used for analysis.

^b Parameter Estimate and P-Value from a longitudinal generalized linear model with identity link function and generalized estimating equations and unstructured covariance structure including mother's max ratio DDD in 3rd trimester, ASM category, child's age, their interaction, and all lower order interactions. Mother's ASM group was not included as a covariate in model.

^c Adjusted for mother's IQ, education level, age at enrollment, smoking during pregnancy, post-birth average BAI score through child's 2YO visit, McMaster FAD problematic family functioning at child's 2YO Visit, and child's sex and small for gestational age status.

^d Based on ASM regimen taken at time of maximum ratio DDD during 3rd trimester.

^e P-value for the interaction between max ratio DDD in 3rd trimester, ASM category, and child's age calculated using the Score test. If significant, the association between max ratio DDD in 3rd trimester and behavior score differs among child's age and ASM category.

eTable 24. Categorical Behavior Scores by Mother’s Study Group and Child’s Age, Children of WWE vs WWoE, Completers Population

	Children of WWE		Children of WWoE		Children of WWE vs WWoE ^a	
Child's Age	N	n (%)	N	n (%)	Odds Ratio (95% CI)	P-Value
Intellectual Disability						
Age 3	278	1 (0.4)	78	0 (0.0)	-	-
Expressive Language Disorder						
Age 3	275	12 (4.4)	79	1 (1.3)	3.6 (0.5, 154.1)	0.312
Receptive Language Disorder						
Age 3	275	9 (3.3)	76	1 (1.3)	2.5 (0.3, 112.7)	0.696
Mixed Expressive/Receptive Language Disorder						
Age 3	274	8 (2.9)	76	1 (1.3)	2.3 (0.3, 101.4)	0.690
BASC-2 Inattentive Presentation ADHD						
Age 2	296	11 (3.7)	90	2 (2.2)	1.7 (0.4, 16.0)	0.741
Age 3	291	8 (2.7)	83	0 (0.0)	-	-
Age 4.5	256	15 (5.9)	74	5 (6.8)	0.9 (0.3, 3.1)	0.784
BASC-2 Combined Presentation ADHD						
Age 2	296	4 (1.4)	90	1 (1.1)	1.2 (0.1, 60.7)	1.000
Age 3	291	4 (1.4)	83	0 (0.0)	-	-
Age 4.5	256	10 (3.9)	74	3 (4.1)	1.0 (0.2, 5.6)	1.000
Autism Spectrum Disorder						
Age 2	306	12 (3.9)	91	1 (1.1)	3.7 (0.5, 158.8)	0.314
Age 3	287	16 (5.6)	81	4 (4.9)	1.1 (0.4, 4.8)	1.000
Age 4.5	257	7 (2.7)	74	4 (5.4)	0.5 (0.1, 2.4)	0.273
PSI-4 Parent Domain At-Risk Score						
Age 2	297	2 (0.7)	89	1 (1.1)	0.6 (0.0, 35.6)	0.546
Age 3	286	4 (1.4)	80	0 (0.0)	-	-

	Children of WWE		Children of WWoE		Children of WWE vs WWoE ^a	
Child's Age	N	n (%)	N	n (%)	Odds Ratio (95% CI)	P-Value
Age 4.5	253	3 (1.2)	74	1 (1.4)	0.9 (0.1, 46.6)	1.000
PSI-4 Child Domain At-Risk Score						
Age 2	299	4 (1.3)	89	1 (1.1)	1.2 (0.1, 59.4)	1.000
Age 3	286	3 (1.0)	80	0 (0.0)	-	-
Age 4.5	254	1 (0.4)	74	4 (5.4)	0.1 (0.0, 0.7)	0.010
PSI-4 Distractibility At-Risk Score						
Age 2	299	38 (12.7)	89	4 (4.5)	3.1 (1.1, 12.3)	0.031
Age 3	286	13 (4.5)	81	3 (3.7)	1.2 (0.3, 6.9)	1.000
Age 4.5	254	16 (6.3)	74	5 (6.8)	0.9 (0.3, 3.4)	1.000
PSI-4 Adaptability At-Risk Score						
Age 2	299	9 (3.0)	89	3 (3.4)	0.9 (0.2, 5.2)	1.000
Age 3	286	8 (2.8)	81	1 (1.2)	2.3 (0.3, 103.4)	0.690
Age 4.5	254	7 (2.8)	74	5 (6.8)	0.4 (0.1, 1.6)	0.151
PSI-4 Reinforces Parent At-Risk Score						
Age 2	299	0 (0.0)	89	0 (0.0)	-	-
Age 3	286	3 (1.0)	81	0 (0.0)	-	-
Age 4.5	254	2 (0.8)	74	0 (0.0)	-	-
PSI-4 Demandingness At-Risk Score						
Age 2	299	11 (3.7)	89	3 (3.4)	1.1 (0.3, 6.2)	1.000
Age 3	286	9 (3.1)	81	1 (1.2)	2.6 (0.4, 115.3)	0.698
Age 4.5	254	3 (1.2)	74	3 (4.1)	0.3 (0.0, 2.2)	0.131
PSI-4 Mood At-Risk Score						
Age 2	299	23 (7.7)	89	9 (10.1)	0.7 (0.3, 1.9)	0.510
Age 3	286	11 (3.8)	81	2 (2.5)	1.6 (0.3, 14.9)	0.741

	Children of WWE		Children of WWoE		Children of WWE vs WWoE ^a	
Child's Age	N	n (%)	N	n (%)	Odds Ratio (95% CI)	P-Value
Age 4.5	254	9 (3.5)	74	7 (9.5)	0.4 (0.1, 1.2)	0.060
PSI-4 Acceptability At-Risk Score						
Age 2	299	0 (0.0)	89	1 (1.1)	-	-
Age 3	286	4 (1.4)	80	0 (0.0)	-	-
Age 4.5	254	0 (0.0)	74	0 (0.0)	-	-
PSI-4 Competence At-Risk Score						
Age 2	299	1 (0.3)	89	1 (1.1)	0.3 (0.0, 23.4)	0.407
Age 3	286	6 (2.1)	80	0 (0.0)	-	-
Age 4.5	254	1 (0.4)	74	1 (1.4)	0.3 (0.0, 23.0)	0.401
PSI-4 Isolation At-Risk Score						
Age 2	297	14 (4.7)	89	1 (1.1)	4.4 (0.6, 186.1)	0.208
Age 3	286	13 (4.5)	81	0 (0.0)	-	-
Age 4.5	254	24 (9.4)	74	4 (5.4)	1.8 (0.6, 7.5)	0.349
PSI-4 Attachment At-Risk Score						
Age 2	297	2 (0.7)	89	1 (1.1)	0.6 (0.0, 35.6)	0.546
Age 3	286	2 (0.7)	81	1 (1.2)	0.6 (0.0, 33.6)	0.528
Age 4.5	254	1 (0.4)	74	0 (0.0)	-	-
PSI-4 Health At-Risk Score						
Age 2	297	20 (6.7)	89	6 (6.7)	1.0 (0.4, 3.1)	1.000
Age 3	286	18 (6.3)	81	2 (2.5)	2.7 (0.6, 24.0)	0.268
Age 4.5	254	41 (16.1)	74	11 (14.9)	1.1 (0.5, 2.5)	0.858
PSI-4 Restriction of Role At-Risk Score						
Age 2	297	29 (9.8)	89	8 (9.0)	1.1 (0.5, 2.9)	1.000
Age 3	286	22 (7.7)	81	4 (4.9)	1.6 (0.5, 6.6)	0.472

	Children of WWE		Children of WWoE		Children of WWE vs WWoE ^a	
Child's Age	N	n (%)	N	n (%)	Odds Ratio (95% CI)	P-Value
Age 4.5	254	12 (4.7)	74	3 (4.1)	1.2 (0.3, 6.7)	1.000
PSI-4 Depression At-Risk Score						
Age 2	297	12 (4.0)	89	3 (3.4)	1.2 (0.3, 6.8)	1.000
Age 3	286	14 (4.9)	81	1 (1.2)	4.1 (0.6, 176.3)	0.207
Age 4.5	254	16 (6.3)	74	2 (2.7)	2.4 (0.5, 22.1)	0.383
PSI-4 Relationship to Spouse At-Risk Score						
Age 2	297	13 (4.4)	89	2 (2.2)	2.0 (0.4, 18.5)	0.536
Age 3	286	18 (6.3)	81	4 (4.9)	1.3 (0.4, 5.4)	0.795
Age 4.5	252	13 (5.2)	74	6 (8.1)	0.6 (0.2, 2.1)	0.396
PSI-4 Life Stress At-Risk Score						
Age 2	297	5 (1.7)	88	3 (3.4)	0.5 (0.1, 3.2)	0.390
Age 3	285	5 (1.8)	80	3 (3.8)	0.5 (0.1, 3.0)	0.380
Age 4.5	254	3 (1.2)	72	2 (2.8)	0.4 (0.0, 5.1)	0.306

N = children with non-missing behavior score. n (%) = number and percentage of children with disability/disorder/at-risk score.

^a Odds of having disability/disorder/at-risk score. Odds Ratio (95% CI) and P-Value from Fisher's Exact Test at each age.

eTable 25. Categorical Behavior Scores by Mother's ASM Category, Children of WWE With 3rd Trimester Blood Levels, Completers Population

Child's Age	Mother's ASM Category ^a											
	Lamotrigine		Levetiracetam		Other Monotherapy		Lamotrigine+ Levetiracetam		Other Polytherapy		All ASMs	
	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)
Intellectual Disability												
Age 3	89	0 (0.0)	69	0 (0.0)	39	1 (2.6)	24	0 (0.0)	27	0 (0.0)	248	1 (0.4)
Expressive Language Disorder												
Age 3	88	3 (3.4)	67	4 (6.0)	39	1 (2.6)	24	2 (8.3)	27	0 (0.0)	245	10 (4.1)
Receptive Language Disorder												
Age 3	88	2 (2.3)	67	2 (3.0)	39	1 (2.6)	24	2 (8.3)	27	1 (3.7)	245	8 (3.3)
Mixed Expressive/Receptive Language Disorder												
Age 3	87	2 (2.3)	67	2 (3.0)	39	1 (2.6)	24	2 (8.3)	27	0 (0.0)	244	7 (2.9)
BASC-2 Inattentive Presentation ADHD												
Age 2	96	4 (4.2)	71	1 (1.4)	44	2 (4.5)	27	0 (0.0)	27	3 (11.1)	265	10 (3.8)
Age 3	94	2 (2.1)	74	3 (4.1)	41	1 (2.4)	24	0 (0.0)	27	1 (3.7)	260	7 (2.7)
Age 4.5	79	4 (5.1)	71	5 (7.0)	33	0 (0.0)	24	2 (8.3)	25	2 (8.0)	232	13 (5.6)
BASC-2 Combined Presentation ADHD												
Age 2	96	2 (2.1)	71	1 (1.4)	44	0 (0.0)	27	0 (0.0)	27	0 (0.0)	265	3 (1.1)
Age 3	94	1 (1.1)	74	1 (1.4)	41	1 (2.4)	24	0 (0.0)	27	0 (0.0)	260	3 (1.2)
Age 4.5	79	3 (3.8)	71	3 (4.2)	33	0 (0.0)	24	1 (4.2)	25	1 (4.0)	232	8 (3.4)
Autism Spectrum Disorder												
Age 2	99	3 (3.0)	73	1 (1.4)	44	4 (9.1)	27	0 (0.0)	28	2 (7.1)	271	10 (3.7)
Age 3	92	3 (3.3)	73	4 (5.5)	41	1 (2.4)	24	2 (8.3)	27	2 (7.4)	257	12 (4.7)
Age 4.5	81	0 (0.0)	71	2 (2.8)	33	1 (3.0)	24	0 (0.0)	25	2 (8.0)	234	5 (2.1)

Child's Age	Mother's ASM Category ^a											
	Lamotrigine		Levetiracetam		Other Monotherapy		Lamotrigine+ Levetiracetam		Other Polytherapy		All ASMs	
	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)
PSI-4 Parent Domain At-Risk Score												
Age 2	95	0 (0.0)	72	0 (0.0)	43	0 (0.0)	26	2 (7.7)	28	0 (0.0)	264	2 (0.8)
Age 3	92	0 (0.0)	70	1 (1.4)	42	0 (0.0)	24	0 (0.0)	27	3 (11.1)	255	4 (1.6)
Age 4.5	80	1 (1.3)	69	0 (0.0)	33	0 (0.0)	23	1 (4.3)	25	1 (4.0)	230	3 (1.3)
PSI-4 Child Domain At-Risk Score												
Age 2	97	1 (1.0)	72	1 (1.4)	43	0 (0.0)	26	1 (3.8)	28	1 (3.6)	266	4 (1.5)
Age 3	92	0 (0.0)	70	1 (1.4)	42	1 (2.4)	24	0 (0.0)	27	1 (3.7)	255	3 (1.2)
Age 4.5	80	0 (0.0)	69	0 (0.0)	33	0 (0.0)	24	1 (4.2)	25	0 (0.0)	231	1 (0.4)
PSI-4 Distractibility At-Risk Score												
Age 2	97	12 (12.4)	72	5 (6.9)	43	5 (11.6)	26	5 (19.2)	28	7 (25.0)	266	34 (12.8)
Age 3	92	4 (4.3)	70	2 (2.9)	42	1 (2.4)	24	1 (4.2)	27	1 (3.7)	255	9 (3.5)
Age 4.5	80	4 (5.0)	69	6 (8.7)	33	0 (0.0)	24	3 (12.5)	25	0 (0.0)	231	13 (5.6)
PSI-4 Adaptability At-Risk Score												
Age 2	97	3 (3.1)	72	2 (2.8)	43	2 (4.7)	26	1 (3.8)	28	0 (0.0)	266	8 (3.0)
Age 3	92	0 (0.0)	70	4 (5.7)	42	1 (2.4)	24	1 (4.2)	27	2 (7.4)	255	8 (3.1)
Age 4.5	80	1 (1.3)	69	3 (4.3)	33	1 (3.0)	24	1 (4.2)	25	1 (4.0)	231	7 (3.0)
PSI-4 Reinforces Parent At-Risk Score												
Age 2	97	0 (0.0)	72	0 (0.0)	43	0 (0.0)	26	0 (0.0)	28	0 (0.0)	266	0 (0.0)
Age 3	92	0 (0.0)	70	1 (1.4)	42	1 (2.4)	24	0 (0.0)	27	1 (3.7)	255	3 (1.2)
Age 4.5	80	0 (0.0)	69	1 (1.4)	33	0 (0.0)	24	1 (4.2)	25	0 (0.0)	231	2 (0.9)
PSI-4 Demandingness At-Risk Score												
Age 2	97	1 (1.0)	72	1 (1.4)	43	0 (0.0)	26	3 (11.5)	28	3 (10.7)	266	8 (3.0)

Child's Age	Mother's ASM Category ^a											
	Lamotrigine		Levetiracetam		Other Monotherapy		Lamotrigine+ Levetiracetam		Other Polytherapy		All ASMs	
	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)
Age 3	92	0 (0.0)	70	4 (5.7)	42	2 (4.8)	24	0 (0.0)	27	1 (3.7)	255	7 (2.7)
Age 4.5	80	1 (1.3)	69	0 (0.0)	33	0 (0.0)	24	1 (4.2)	25	1 (4.0)	231	3 (1.3)
PSI-4 Mood At-Risk Score												
Age 2	97	5 (5.2)	72	6 (8.3)	43	3 (7.0)	26	6 (23.1)	28	1 (3.6)	266	21 (7.9)
Age 3	92	2 (2.2)	70	6 (8.6)	42	2 (4.8)	24	0 (0.0)	27	0 (0.0)	255	10 (3.9)
Age 4.5	80	2 (2.5)	69	3 (4.3)	33	0 (0.0)	24	2 (8.3)	25	0 (0.0)	231	7 (3.0)
PSI-4 Acceptability At-Risk Score												
Age 2	97	0 (0.0)	72	0 (0.0)	43	0 (0.0)	26	0 (0.0)	28	0 (0.0)	266	0 (0.0)
Age 3	92	0 (0.0)	70	2 (2.9)	42	1 (2.4)	24	0 (0.0)	27	1 (3.7)	255	4 (1.6)
Age 4.5	80	0 (0.0)	69	0 (0.0)	33	0 (0.0)	24	0 (0.0)	25	0 (0.0)	231	0 (0.0)
PSI-4 Competence At-Risk Score												
Age 2	97	0 (0.0)	72	0 (0.0)	43	0 (0.0)	26	1 (3.8)	28	0 (0.0)	266	1 (0.4)
Age 3	92	0 (0.0)	70	1 (1.4)	42	1 (2.4)	24	1 (4.2)	27	3 (11.1)	255	6 (2.4)
Age 4.5	80	0 (0.0)	69	0 (0.0)	33	0 (0.0)	24	1 (4.2)	25	0 (0.0)	231	1 (0.4)
PSI-4 Isolation At-Risk Score												
Age 2	95	1 (1.1)	72	3 (4.2)	43	0 (0.0)	26	2 (7.7)	28	4 (14.3)	264	10 (3.8)
Age 3	92	0 (0.0)	70	5 (7.1)	42	0 (0.0)	24	2 (8.3)	27	2 (7.4)	255	9 (3.5)
Age 4.5	80	2 (2.5)	69	7 (10.1)	33	4 (12.1)	24	5 (20.8)	25	3 (12.0)	231	21 (9.1)
PSI-4 Attachment At-Risk Score												
Age 2	95	0 (0.0)	72	1 (1.4)	43	0 (0.0)	26	0 (0.0)	28	1 (3.6)	264	2 (0.8)
Age 3	92	0 (0.0)	70	1 (1.4)	42	0 (0.0)	24	0 (0.0)	27	1 (3.7)	255	2 (0.8)
Age 4.5	80	0 (0.0)	69	0 (0.0)	33	0 (0.0)	24	1 (4.2)	25	0 (0.0)	231	1 (0.4)

Child's Age	Mother's ASM Category ^a											All ASMs	
	Lamotrigine		Levetiracetam		Other Monotherapy		Lamotrigine+ Levetiracetam		Other Polytherapy				
	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)	N	n (%)	
PSI-4 Health At-Risk Score													
Age 2	95	3 (3.2)	72	6 (8.3)	43	3 (7.0)	26	3 (11.5)	28	3 (10.7)	264	18 (6.8)	
Age 3	92	2 (2.2)	70	4 (5.7)	42	3 (7.1)	24	4 (16.7)	27	4 (14.8)	255	17 (6.7)	
Age 4.5	80	8 (10.0)	69	16 (23.2)	33	4 (12.1)	24	3 (12.5)	25	5 (20.0)	231	36 (15.6)	
PSI-4 Restriction of Role At-Risk Score													
Age 2	95	7 (7.4)	72	6 (8.3)	43	2 (4.7)	26	5 (19.2)	28	7 (25.0)	264	27 (10.2)	
Age 3	92	5 (5.4)	70	7 (10.0)	42	0 (0.0)	24	3 (12.5)	27	4 (14.8)	255	19 (7.5)	
Age 4.5	80	2 (2.5)	69	1 (1.4)	33	0 (0.0)	24	2 (8.3)	25	4 (16.0)	231	9 (3.9)	
PSI-4 Depression At-Risk Score													
Age 2	95	3 (3.2)	72	4 (5.6)	43	0 (0.0)	26	4 (15.4)	28	0 (0.0)	264	11 (4.2)	
Age 3	92	3 (3.3)	70	5 (7.1)	42	1 (2.4)	24	1 (4.2)	27	3 (11.1)	255	13 (5.1)	
Age 4.5	80	4 (5.0)	69	5 (7.2)	33	1 (3.0)	24	3 (12.5)	25	2 (8.0)	231	15 (6.5)	
PSI-4 Relationship to Spouse At-Risk Score													
Age 2	95	6 (6.3)	72	2 (2.8)	43	0 (0.0)	26	3 (11.5)	28	1 (3.6)	264	12 (4.5)	
Age 3	92	8 (8.7)	70	3 (4.3)	42	2 (4.8)	24	1 (4.2)	27	3 (11.1)	255	17 (6.7)	
Age 4.5	79	5 (6.3)	69	1 (1.4)	33	2 (6.1)	23	1 (4.3)	25	4 (16.0)	229	13 (5.7)	
PSI-4 Life Stress At-Risk Score													
Age 2	95	2 (2.1)	72	0 (0.0)	43	1 (2.3)	26	2 (7.7)	28	0 (0.0)	264	5 (1.9)	
Age 3	92	0 (0.0)	70	3 (4.3)	41	0 (0.0)	24	0 (0.0)	27	0 (0.0)	254	3 (1.2)	
Age 4.5	80	0 (0.0)	69	1 (1.4)	33	0 (0.0)	24	1 (4.2)	25	1 (4.0)	231	3 (1.3)	

Notes: N = children with non-missing behavior score by ASM category. n = number and percent of children with disability/disorder/at-risk score within each ASM category.

^a ASM at time of maximum observed 3rd trimester ratio ASM concentration (includes day of delivery).

eTable 26. Demographic, Baseline Characteristics, and Risk Factors for Children Included vs Excluded From Primary Analysis 1, Categorical Variables, Children in Primary Analysis 1, N = 451

	Children Included, N = 386	Children Excluded, N = 65	
	n (%)	n (%)	P-Value^a
Mother's Study Group			0.040
WWE	302 (78.2)	43 (66.2)	
WWoE	84 (21.8)	22 (33.8)	
Child's Sex			1.000
Female	198 (51.3)	33 (50.8)	
Male	188 (48.7)	32 (49.2)	
Child's Race			0.303
White	298 (77.2)	51 (78.5)	
Black or African American	26 (6.7)	7 (10.8)	
Other/Unknown	62 (16.1)	7 (10.8)	
Child's Ethnicity - Hispanic or Latino	77 (19.9)	17 (26.2)	0.252
Twin	29 (7.5)	7 (10.8)	0.332
Small for Gestational Age (SGA)	24 (6.4)	3 (5.7)	1.000
Missing	9	12	
Major Congenital Malformations	19 (4.9)	1 (1.5)	0.334
Any Breastfeeding	307 (79.7)	36 (65.5)	0.023
Missing	1	10	
Periconceptional Folate Use	324 (83.9)	44 (67.7)	0.003
Periconceptional Folate Dose			0.009
0 mg	62 (16.3)	21 (33.9)	
> 0 - 0.4 mg	38 (10.0)	1 (1.6)	
> 0.4 - 1 mg	90 (23.6)	13 (21.0)	

	Children Included, N = 386	Children Excluded, N = 65	
	n (%)	n (%)	P-Value^a
> 1 - 4 mg	169 (44.4)	25 (40.3)	
> 4 mg	22 (5.8)	2 (3.2)	
Missing	5	3	
Pregnancy Planned/Welcomed			0.006
Planned	276 (71.5)	35 (53.8)	
Unplanned/Welcome	98 (25.4)	29 (44.6)	
Unplanned/Unwelcome	12 (3.1)	1 (1.5)	
Major Depressive Episode During Pregnancy^b	13 (3.4)	6 (9.2)	0.042
Mother's Education			0.011
College Degree (Advanced)	112 (29.0)	9 (13.8)	
College Degree (Not Advanced)	169 (43.8)	29 (44.6)	
No College Degree	105 (27.2)	27 (41.5)	
Mother's Employment			<.001
Employed full-time	215 (55.7)	30 (46.2)	
Employed part-time	62 (16.1)	3 (4.6)	
Unemployed ^c	109 (28.2)	32 (49.2)	
Household Income			<.001
Subject desires not to answer	21 (5.4)	12 (18.5)	
\$24,999 or less	65 (16.8)	13 (20.0)	
\$25,000-49,999	40 (10.4)	10 (15.4)	
\$50,000-74,999	52 (13.5)	11 (16.9)	
\$75,000-99,999	70 (18.1)	3 (4.6)	
\$100,000 and up	138 (35.8)	16 (24.6)	
Smoking^d	24 (6.2)	5 (7.7)	0.590

	Children Included, N = 386	Children Excluded, N = 65	
	n (%)	n (%)	P-Value^a
Alcohol Use^d	102 (26.4)	15 (23.1)	0.648
Illicit Substance Use^d	13 (3.4)	1 (1.6)	0.703
Missing	2	1	
McMaster FAD Problematic Family Functioning at Child's 2YO Visit	65 (17.7)	9 (39.1)	0.023
Missing	18	42	
Lifetime History of Mood Disorder^e	60 (15.9)	12 (22.6)	0.238
Missing	8	12	
Lifetime History of Anxiety Disorder^e	59 (15.6)	7 (13.2)	0.839
Missing	8	12	

Notes: Missing not used in calculation of percentages or in p-values. FAD = Family Assessment Device

^a P-Values from Fisher's Exact Test.

^b Depression based on SCID Mood Module at any depression assessment during pregnancy.

^c Unemployed includes stay at home parent without outside job, unemployed due to disability, full-time student and looking for work.

^d Self-reported smoking, alcohol use, or illicit substance use (including marijuana) at any time during pregnancy.

^e Diagnosis from SCID.

eTable 27. Demographic, Baseline Characteristics, and Risk Factors for Children Included vs Excluded From Primary Analysis 1, Continuous Variables, Children in Primary Analysis 1, N = 451

	Children Included, N = 386			Children Excluded, N = 65			P-Value ^a
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)	
WGA at Birth	386	38.5 (38.3, 38.7)	39 [24, 43]	65	38.2 (37.8, 38.7)	39 [31, 42]	0.388
WGA at Enrollment	386	13.9 (13.4, 14.3)	14 [4, 29]	65	15.7 (14.7, 16.7)	17 [6, 23]	0.003
Birthweight (kg)	379	3.23 (3.17, 3.29)	3.3 [0.6, 5.0]	54	3.13 (2.94, 3.32)	3.1 [1.2, 4.6]	0.255
Mother's Age at Enrollment	386	30.6 (30.1, 31.1)	31 [15, 46]	65	29.6 (28.0, 31.1)	29 [17, 43]	0.136
Mother's IQ	386	99.6 (98.3, 100.9)	101 [58, 131]	64	95.9 (92.3, 99.4)	95 [58, 125]	0.034
Father's IQ ^b	250	104.1 (102.4, 105.8)	104 [58, 139]	32	101.2 (95.7, 106.6)	103 [63, 140]	0.253
Maternal Relative's IQ ^b	140	101.3 (98.7, 103.8)	103 [51, 133]	13	91.7 (83.7, 99.7)	95 [68, 115]	0.030
BDI During Pregnancy ^c	386	6.83 (6.29, 7.37)	5.5 [0.0, 38.7]	65	8.38 (7.23, 9.54)	8.0 [0.0, 21.7]	0.001
BAI During Pregnancy ^c	386	6.09 (5.53, 6.65)	4.7 [0.0, 38.3]	65	7.18 (5.88, 8.49)	5.7 [0.5, 23.0]	0.051
PSS During Pregnancy ^c	386	17.61 (16.91, 18.31)	17.3 [2.7, 40.0]	65	19.74 (18.08, 21.39)	18.7 [7.0, 33.3]	0.022
PSQI During Pregnancy ^{bd}	351	5.54 (5.23, 5.84)	5.0 [0.0, 15.5]	55	6.24 (5.43, 7.05)	5.8 [0.7, 15.8]	0.100

	Children Included, N = 386			Children Excluded, N = 65			
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)	P-Value ^a

Note: WGA = weeks gestational age; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; PSS = Perceived Stress Scale; PSQI = Pittsburgh Sleep Quality Index.

^a P-Values from T-Test (WGA at Birth, WGA at Enrollment, Birthweight, Age, IQ Scores, PSQI Scores) and Wilcoxon Rank-Sum Test (BDI, BAI, and PSS Scores).

^b Father's IQ, Maternal Relative's IQ, and PSQI Scores not assessed for inclusion in imputation model due to extensive missing data.

^c Average of all assessments completed during time period. Pregnancy: enrollment through day of delivery; Post-Birth: post-delivery through 2YO visit. Average scores during Post-Birth and Enrollment through 2YO visit excluded due to insufficient data in the Excluded population to calculate the average score during Post-Birth period.

^d Weighted monthly average of PSQI assessments completed during time period. At most one PSQI score per day was used in the calculation. Pregnancy: Enrollment through the day before delivery; Average scores during Postpartum and Pregnancy+Postpartum excluded due to insufficient data in the Excluded population to calculate the average score during Postpartum period.

eTable 28. Outcomes for Children Included vs Excluded From Primary Analysis 1, All Children, N = 451

ABAS-3 General Adaptive Composite Score	Children Included, N = 386			Children Excluded, N = 65		
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)
Age 4.5	326	101.1 (99.8, 102.4)	101 [49, 120]	1	91.0 (NC)	91 [91, 91]
Age 3	372	106.7 (105.5, 108.0)	108 [61, 120]	2	106.5 (74.7, 138.3)	107 [104, 109]

Note: Statistical test to compare groups not computed due to larger number of missing due to drop out in the Excluded population. NC = Not calculable.

eTable 29. Demographic, Baseline Characteristics, and Risk Factors for Children Included vs Excluded From Primary Analysis 2, Categorical Variables, Children of WWE on ASM in 3rd Trimester, N = 329

	Children Included, N = 271	Children Excluded, N = 58	
	n (%)	n (%)	P-Value^a
Child's Sex			0.469
Female	143 (52.8)	27 (46.6)	
Male	128 (47.2)	31 (53.4)	
Child's Race			0.505
White	223 (82.3)	45 (77.6)	
Black or African American	11 (4.1)	4 (6.9)	
Other/Unknown	37 (13.7)	9 (15.5)	
Child's Ethnicity - Hispanic or Latino	54 (19.9)	13 (22.4)	0.720
Twin	19 (7.0)	9 (15.5)	0.064
Small for Gestational Age (SGA)	15 (5.7)	3 (6.3)	0.745
Missing	6	10	
Major Congenital Malformations	13 (4.8)	3 (5.2)	1.000
Any Breastfeeding	208 (77.0)	29 (55.8)	0.003
Missing	1	6	
Periconceptual Folate Use	239 (88.2)	44 (75.9)	0.021
Periconceptual Folate Dose			0.113
0 mg	32 (11.9)	14 (25.5)	
> 0 - 0.4 mg	19 (7.0)	3 (5.5)	
> 0.4 - 1 mg	51 (18.9)	7 (12.7)	
> 1 - 4 mg	146 (54.1)	29 (52.7)	
> 4 mg	22 (8.1)	2 (3.6)	
Missing	1	3	

	Children Included, N = 271	Children Excluded, N = 58	
	n (%)	n (%)	P-Value^a
Pregnancy Planned/Welcomed			0.001
Planned	200 (73.8)	29 (50.0)	
Unplanned/Welcomed	63 (23.2)	27 (46.6)	
Unplanned/Unwelcomed	8 (3.0)	2 (3.4)	
Major Depressive Episode During Pregnancy^b	11 (4.1)	4 (6.9)	0.313
Mother's Education			0.008
College Degree (Advanced)	75 (27.7)	7 (12.1)	
College Degree (Not Advanced)	126 (46.5)	26 (44.8)	
No College Degree	70 (25.8)	25 (43.1)	
Mother's Employment			<.001
Employed full-time	158 (58.3)	19 (32.8)	
Employed part-time	41 (15.1)	3 (5.2)	
Unemployed ^c	72 (26.6)	36 (62.1)	
Household Income			<.001
Subject desires not to answer	11 (4.1)	12 (20.7)	
\$24,999 or less	45 (16.6)	13 (22.4)	
\$25,000-49,999	28 (10.3)	5 (8.6)	
\$50,000-74,999	37 (13.7)	10 (17.2)	
\$75,000-99,999	48 (17.7)	6 (10.3)	
\$100,000 and up	102 (37.6)	12 (20.7)	
Smoking^d	14 (5.2)	9 (15.5)	0.010
Alcohol Use^d	64 (23.6)	14 (24.1)	1.000
Illicit Substance Use^d	8 (3.0)	2 (3.5)	0.688
Missing	1	1	

	Children Included, N = 271	Children Excluded, N = 58	
	n (%)	n (%)	P-Value^a
McMaster FAD Problematic Family Functioning at Child's 2YO Visit	48 (18.7)	9 (28.1)	0.238
Missing	14	26	
Lifetime History of Mood Disorder^e	41 (15.4)	12 (25.5)	0.093
Missing	4	11	
Lifetime History of Anxiety Disorder^e	39 (14.6)	6 (12.8)	1.000
Missing	4	11	
Seizure Type^f			0.586
Focal	87 (32.1)	20 (34.5)	
Generalized	164 (60.5)	32 (55.2)	
Unclassified/Mixed	20 (7.4)	6 (10.3)	
5 or More Convulsions During Pregnancy	9 (3.3)	8 (15.1)	0.002
Missing	1	5	
Mother's 3rd Trimester ASM^g			
Monotherapy	219 (80.8)	35 (60.3)	0.002 ^h
Lamotrigine	98 (36.2)	10 (17.2)	0.005 ⁱ
Levetiracetam	77 (28.4)	15 (25.9)	
Oxcarbazepine	14 (5.2)	2 (3.4)	
Carbamazepine	10 (3.7)	3 (5.2)	
Zonisamide	10 (3.7)	3 (5.2)	
Other	10 (3.7)	2 (3.4)	
Polytherapy	52 (19.2)	23 (39.7)	
Lamotrigine + Levetiracetam	25 (9.2)	9 (15.5)	
Other	27 (10.0)	14 (24.1)	

	Children Included, N = 271	Children Excluded, N = 58	
	n (%)	n (%)	P-Value^a

Notes: Missing not used in calculation of percentages or in p-values. FAD = Family Assessment Device

^a P-Values from Fisher's Exact Test.

^b Depression based on SCID Mood Module at any depression assessment during pregnancy.

^c Unemployed includes stay at home parent without outside job, unemployed due to disability, full-time student and looking for work.

^d Self-reported smoking, alcohol use, or illicit substance use (including marijuana) at any time during pregnancy.

^e Diagnosis from SCID.

^f Three children in the Included population had mothers who reported multiple seizure types, 2 reported generalized & focal seizures and 1 reported generalized & unclassified seizures.

^g Mother's ASM regimen at time of blood draw for maximum observed ratio ASM concentration during 3rd trimester (includes day of delivery) or if missing ASM concentration then ASM regimen for maximum ratio DDD during 3rd trimester.

^h Mother's ASM Group (Monotherapy, Polytherapy) by Included vs Excluded.

ⁱ Mother's ASM Category (Lamotrigine, Levetiracetam, Other Monotherapy, Lamotrigine + Levetiracetam, Other Polytherapy) by Included vs Excluded.

eTable 30. Demographic, Baseline Characteristics, and Risk Factors for Children Included vs Excluded From Primary Analysis 2, Continuous Variables, Children of WWE on ASM in 3rd Trimester, N = 329

	Children Included, N = 271			Children Excluded, N = 58			P-Value ^a
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)	
WGA at Birth	271	38.6 (38.4, 38.8)	39 [33, 42]	58	37.6 (36.9, 38.3)	38 [29, 41]	<.001
WGA at Enrollment	271	13.4 (12.8, 13.9)	14 [4, 29]	58	15.2 (14.0, 16.4)	17 [6, 23]	0.006
Birthweight (kg)	266	3.27 (3.20, 3.33)	3.3 [1.7, 4.9]	48	2.90 (2.68, 3.13)	3.1 [1.1, 4.3]	<.001
Mother's Age at Enrollment	271	31.0 (30.4, 31.6)	31 [18, 46]	58	29.1 (27.3, 30.8)	29 [17, 43]	0.009
Mother's IQ	271	98.8 (97.3, 100.3)	100 [65, 124]	57	93.1 (89.1, 97.1)	95 [58, 124]	0.002
Father's IQ ^b	189	104.6 (102.7, 106.6)	105 [58, 139]	20	99.2 (92.0, 106.3)	98 [63, 140]	0.094
Maternal Relative's IQ ^b	100	101.5 (98.4, 104.7)	104 [51, 133]	15	90.4 (83.8, 97.0)	88 [68, 113]	0.011
BDI During Pregnancy ^c	271	6.91 (6.22, 7.60)	5.3 [0.0, 38.7]	58	9.20 (7.96, 10.44)	8.2 [0.0, 21.7]	<.001
BAI During Pregnancy ^c	271	6.18 (5.50, 6.86)	4.7 [0.0, 38.3]	58	8.59 (6.93, 10.26)	6.8 [0.5, 23.0]	0.007
PSS During Pregnancy ^c	271	17.71 (16.84, 18.58)	17.3 [2.7, 40.0]	58	21.03 (19.28, 22.78)	20.5 [7.0, 34.5]	<.001
PSQI During Pregnancy ^{bd}	248	5.69 (5.31, 6.06)	5.1 [0.0, 15.5]	47	6.63 (5.78, 7.49)	6.0 [3.0, 15.8]	0.048
Convulsions During Pregnancy	270	0.6 (0.3, 0.9)	0 [0, 28]	53	2.7 (0.6, 4.8)	0 [0, 44]	0.075
Max Observed Ratio ASM Concentration During 3rd Trimester ^e	271	0.52 (0.48, 0.56)	0.4 [0.0, 1.9]	32	0.57 (0.45, 0.68)	0.5 [0.0, 1.6]	0.490

	Children Included, N = 271			Children Excluded, N = 58			P-Value ^a
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)	
Max Ratio DDD During 3rd Trimester ^f	271	2.21 (2.05, 2.38)	2.0 [0.2, 8.3]	58	2.71 (2.13, 3.30)	2.0 [0.3, 10.7]	0.366

Note: WGA = weeks gestational age; BDI = Beck Depression Inventory; BAI = Beck Anxiety Inventory; PSS = Perceived Stress Scale; PSQI = Pittsburgh Sleep Quality Index.

^a P-Values from T-Test (WGA at Birth, WGA at Enrollment, Birthweight, Age, IQ Scores, PSQI Scores) and Wilcoxon Rank-Sum Test (BDI, BAI, and PSS Scores, Convulsions, ratio DDD).

^b Father's IQ, Maternal Relative's IQ, and PSQI Scores not assessed for inclusion in imputation model due to extensive missing data.

^c Average of all assessments completed during time period. Pregnancy: enrollment through day of delivery; Post-Birth: post-delivery through 2YO visit. Average scores during Post-Birth and Enrollment through 2YO visit excluded due to insufficient data in the Excluded population to calculate the average score during Post-Birth period.

^d Weighted monthly average of PSQI assessments completed during time period. At most one PSQI score per day was used in the calculation. Pregnancy: Enrollment through the day before delivery; Average scores during Postpartum and Pregnancy+Postpartum excluded due to insufficient data in the Excluded population to calculate the average score during Postpartum period.

^e Ratio ASM Concentration calculated as ratio upper limit for therapeutic range. For mothers on polytherapy, ratio ASM concentration calculated by summing the ratio ASM concentration for each ASM. Maximum observed value recorded during 3rd trimester, including day of delivery.

^f Ratio DDD = Ratio Defined Daily Dose, calculated by dividing the mother's ASM total prescribed daily dose by the WHO defined daily dose values. For mothers on polytherapy, ratio DDD equals the sum across the ratio DDD for all ASMs.

eTable 31. Outcomes for Children Included vs Excluded From Primary Analysis 2, Children of WWE on ASM in 3rd Trimester, N = 329

ABAS-3 General Adaptive Composite Score	Children Included, N = 271			Children Excluded, N = 58		
	N	Mean (95% CI)	Median (Min, Max)	N	Mean (95% CI)	Median (Min, Max)
Age 4.5	229	101.2 (99.6, 102.8)	101 [49, 120]	11	98.5 (90.9, 106.0)	96 [85, 118]
Age 3	261	106.6 (105.0, 108.1)	108 [61, 120]	18	102.6 (96.0, 109.2)	100 [81, 120]

Note: Statistical test to compare groups not computed due to larger number of missing in the Excluded population.

eTable 32. Age 4.5 ABAS-3 General Adaptive Composite Score by Mother’s Study Group – Sensitivity Analysis, Children of WWE and WWoE

Sensitivity Analysis/ Mother's Study Group	Unadjusted Analysis ^a			Adjusted Analysis ^b		
	N	Mean (95% CI)	P-value	N	LS Mean (95% CI)	P-value
1. Completers Analysis^c						
WWE	253	101.3 (99.8, 102.8)	0.594	248	101.3 (99.9, 102.6)	0.650
WWoE	73	100.4 (97.6, 103.3)		73	100.6 (98.0, 103.1)	
2. All Subject Imputation Analysis^d						
WWE	345	100.9 (99.5, 102.4)	0.860	345	101.1 (99.7, 102.5)	0.878
WWoE	106	101.2 (98.5, 103.9)		106	100.8 (98.2, 103.5)	
3. Birth-Related Covariates Excluded from Adjusted Model^e						
WWE	-	-	-	302	101.5 (100.0, 102.9)	0.720
WWoE	-	-		84	100.9 (98.3, 103.5)	

Notes: N = children included in sensitivity analysis.

^a Linear regression model.

^b Linear regression model adjusted for mother's IQ, education level, age at enrollment, illicit drug-use during pregnancy, major depressive episode during pregnancy, post-birth average PSS score, and child's sex, birthweight, and small for gestational age status. Birthweight and small for gestational age status not included in adjusted model for sensitivity analysis 3.

^c Children with non-missing age 4.5 ABAS-3 general adaptive composite scores.

^d All children enrolled in study, missing age 4.5 ABAS-3 General Adaptive Composite Scores imputed using multiple imputation.

^e Rerun of the primary analysis model excluding birth-related covariates: child's birthweight and small for gestational age status. Includes children with Age 4.5 ABAS-3 General Adaptive Composite Score or age 3 ABAS-3 General Adaptive Composite Score. Missing Age 4.5 ABAS-3 General Adaptive Composite Scores imputed using multiple imputation.

eTable 33. Association Between Age 4.5 ABAS-3 General Adaptive Composite Score and Maximum Observed Ratio ASM Concentration^a During 3rd Trimester – Sensitivity Analysis, Children of WWE on ASM During the 3rd Trimester

Sensitivity Analysis/ Outcome	Unadjusted Analysis ^b			Adjusted Analysis ^c		
	N	Parameter Estimate (95% CI)	P-value	N	Parameter Estimate (95% CI)	P-value
1. Completers Analysis^c						
Mother's 3rd Trimester Max Observed Ratio ASM Concentration ^a	229	-8.17 (-12.36, - 3.97)	<.001	217	-9.46 (-14.31, - 4.62)	<.001
2. All Subject Imputation Analysis^d						
Mother's 3rd Trimester Max Observed Ratio ASM Concentration ^a	329	-6.3 (-10.5, -2.1)	0.003	329	-6.4 (-11.4, -1.4)	0.012
3. Birth-Related Covariates Excluded from Adjusted Model^e						
Mother's 3rd Trimester Max Observed Ratio ASM Concentration ^a	-	-	-	271	-7.7 (-12.4, -2.9)	0.002

Notes: N = children included in sensitivity analysis.

^a Ratio ASM Concentration calculated as ratio upper limit for therapeutic range. For mothers on polytherapy, ratio ASM concentration calculated by summing the ratio ASM concentration for each ASM. Maximum observed value recorded during 3rd trimester, including day of delivery.

^b Linear regression model.

^c Linear regression model adjusted for mother's IQ, education level, age at enrollment, ASM Group (monotherapy/polytherapy), smoking during pregnancy, post-birth average BAI score, McMaster FAD problematic family functioning at Child's 2YO Visit, and child's sex and small for gestational age status. Small for gestational age status not included in adjusted model for sensitivity analysis 3.

^d Children with Age 4.5 ABAS-3 General Adaptive Composite Score and mother with 3rd trimester ASM blood levels.

^d All children of WWE on ASM during the 3rd trimester enrolled in study, missing age 4.5 ABAS-3 General Adaptive Composite Scores imputed using multiple imputation.

^e Rerun of the primary analysis model excluding birth-related covariates: child's small for gestational age status. Includes children with Age 4.5 ABAS-3 General Adaptive Composite Score or age 3 ABAS-3 General Adaptive Composite Score and mother with 3rd trimester ASM blood levels. Missing Age 4.5 ABAS-3 General Adaptive Composite Scores imputed using multiple imputation.

eTable 34. Summary of Age 4.5 ABAS-3 General Adaptive Composite Score by Mother’s Study Group and Pregnancy ASM Status, Children of WWE and WWoE, Completers Population, N = 326

Mother's Study Group and Pregnancy ASM Status	N	Mean (95% CI)	Median [Min, Max]
WWE on ASM During Pregnancy	240	101.1 (99.6, 102.6)	100.5 [49.0, 120.0]
WWE Not on ASM During Pregnancy	13	104.3 (97.0, 111.6)	106.0 [88.0, 120.0]
WWoE	73	100.4 (97.6, 103.3)	101.0 [52.0, 120.0]

Notes: N = children with non-missing age 4.5 ABAS-3 General Adaptive Composite score.

eTable 35. Age 4.5 ABAS-3 General Adaptive Composite Score by Mother's Study Group - Sensitivity Analysis Excluding Children of WWE Not on ASM During Pregnancy, Children of WWE on ASM During Pregnancy and WWoE, Completers Population, N = 313

		Unadjusted Analysis ^a		Adjusted Analysis ^b	
Mother's Study Group	N	Mean (95% CI)	P-value	LS Mean (95% CI)	P-value
WWE on ASM During Pregnancy	240	101.1 (99.6, 102.6)	0.668	101.2 (99.8, 102.6)	0.677
WWoE	73	100.4 (97.6, 103.3)		100.5 (98.0, 103.1)	

Notes: N = children with non-missing age 4.5 ABAS-3 General Adaptive Composite scores, excluding children of WWE not on ASM during pregnancy.

^a Mean and P-value from a linear regression model.

^b Linear regression model adjusted for mother's IQ, education level, age at enrollment, illicit drug-use during pregnancy, major depressive episode during pregnancy, post-birth average PSS score, and child's sex, birthweight, and small for gestational age status.