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Supplementary Material

- Article Title: Correlating Psychotropic Use to Major Depressive Disorder and ADHD Research Diagnoses: Trends in a Prospective Pediatric Cohort From Ages 3 to 21
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Supplementary Material Appendix 1.

Supplementary Methods:

We used generalized estimating equations (GEE) to investigate the probability of psychotropic medication use over the course of the study. The GEE models had a binomial distribution with a logit link function and assumed an independent correlation matrix. GEE is ideal for dealing with repeated measurements and missing data. The dependent variables in these models were dichotomous variables indicating whether medication (any psychotropic, ADHD medication, antidepressants, and antipsychotics) was prescribed at each assessment. Independent variables were time-varying PECFAS/CAFAS score, ADHD severity, MDD severity, or ODD/CD severity. Age was the time variable, age squared was included if significant, and covariates were sex and time-varying income-to-needs ratio. The interaction between the independent variable and age was entered into the model but then removed if non-significant to obtain the final model. FDR correction was applied to the GEE models by correcting across all main effects of the independent variable and again across all age by independent variable interactions.

Supplementary Results:

We looked at the probability of psychotropic prescription over time as a function of impairment or disease severity (Supplementary Figure 1). In general, children with higher impairment levels had a significantly higher probability of receiving a psychotropic prescription. This pattern held true when looking at psychotropics separately: children with higher impairment levels also had a significantly higher probability of receiving ADHD medications, antidepressants, and antipsychotics. When looking at psychotropic prescription as a function of disease severity, we also observed some significant relationships. The probability of antidepressant prescription was significantly increased with increased MDD severity score, the probability of ADHD medication prescription was significantly increased with increased ADHD severity score, and the probability of antipsychotic prescription was significantly increased with increased with

Antidepressants	Antipsychotics	ADHD Medications	Antimanic	Anti-Anxiety
Amitriptyline	Aripiprazole	Amphetamine	Carbamazepine	Buspirone
Bupropion	Chlorprothixene	Atomoxetine	Lamotrigine	Clonazepam
Citalopram	Clozapine	Clonidine	Lithium	
Clomipramine	Haloperidol	Dexmethylphenidate	Oxcarbazepine	
Desipramine	Lurasidone	Guanfacine	Valproic acid	
Doxepin	Mesoridazine	Lisdexamfetamine		
Duloxetine	Olanzapine	Methylphenidate		
Escitalopram	Paliperidone			
Fluoxetine	Prochlorperazine			
Imipramine	Quetiapine			
Mirtazapine	Risperidone			
Nortriptyline	Ziprasidone			
Paroxetine				
Sertraline				
Trazodone				
Venlafaxine				

Supplementary Table 1. Complete list of psychotropics reported.

Abbreviations: ADHD = attention-deficit/hyperactivity disorder.

Supplementary Table 2. Baseline subject characteristics by number of age groups with	I
assessments.	

	1 Age Group (N=39)		2 Age Groups (N=152)		3 Age Groups (N=157)		Omnibus Test	
Subject Characteristics	Mean	SD	Mean	SD	Mean	SD	F	р*
Age at first wave	4.88	2.27	5.90	2.67	4.51	0.79	19.11	<0.0001
First income-to-needs ratio	1.78	1.15	2.05	1.11	2.06	1.18	0.96	0.3848
	%	Ν	%	Ν	%	Ν	χ²	р
Female sex	51.3	20	45.4	69	50.3	79	0.91	0.6351
Race							0.46	0.7958
White	38.5	15	54.0	82	55.4	87		
Black	43.6	17	34.2	52	32.5	51		
Other	17.9	7	11.8	18	12.1	19		

*Differences were considered significant if p < 0.05 (shown in bold).

Abbreviations: SD = standard deviation.

	Preschool (N=302)		School-Age (N=316)		Adolescent (N=196)	
Medication	% N		%	N	%	N
Any psychotropic	9.3	28	26.0	82	32.1	63
Antipsychotic	4.0	12	8.5	27	5.6	11
Antianxiety	0.0	0	1.0	3	4.6	9
Antidepressant	0.0	0	9.2	29	17.4	34
Non-antipsychotic mood stabilizer	0.7	2	4.1	13	3.6	7
ADHD medication	6.3	19	23.7	75	23.0	45
Alpha-agonist	1.7	5	7.0	22	2.0	4
Stimulant	4.3	13	23.1	73	22.5	44
Strattera	1.0	3	5.4	17	1.0	2

Supplementary Table 3. Rates of All Psychotropic Medication Use by Age Group

Abbreviations: ADHD = attention-deficit/hyperactivity disorder.

	Non-Pha	Non-Pharmacologic Therapy				
Preschool	Total N	%	N			
All children	301	24.9	75			
Any research diagnosis	184	35.3	65			
MDD	95	43.2	41			
ADHD	58	60.3	35			
Any psychotropic mediation	28	89.3	25			
Antidepressants	0	0.0	0			
ADHD medication	19	89.5	17			
Antipsychotics	12	100.0	12			
	Non-Pha	rmacologio	: Therapy			
School-Age	Total N	%	N			
All children	316	50.0	158			
Any research diagnosis	200	65.0	130			
MDD	111	76.6	85			
ADHD	78	85.9	67			
Any psychotropic mediation	82	96.3	79			
Antidepressants	29	100.0	29			
ADHD medication	75	97.3	73			
Antipsychotics	27	100.0	27			
	Non-Pha	Non-Pharmacologic Therapy				
Adolescent/Early Adult	Total N	%	N			
All children	195	50.3	98			
Any research diagnosis	112	68.8	77			
MDD	47	80.9	38			
ADHD	25	80.0	20			
Any psychotropic mediation	63	79.4	50			
Antidepressants	34	91.2	31			
ADHD medication	45	77.8	35			
Antipsychotics	11	100.0	11			

Supplementary Table 4. Rates of Non-Pharmacologic Therapy by Age Group.

Abbreviations: MDD = major depressive disorder, ADHD = attention-deficit/hyperactivity disorder.

Supplementary Table 5. Psychotropic use in participants without a corresponding research diagnosis

		No ADHD Meds		ADHD Meds		
	Total N	N	%	N	%	
No Preschool ADHD	244	237	97.1	7	2.9	
		N Antidep	No Antidepressants		ressants	
	Total N	N	%	N	%	
No Preschool MDD or Anxiety	161	161	100%	0	0%	
		No ADH	No ADHD Meds		ADHD Meds	
	Total N	N	%	N	%	
No School-Age ADHD	237	214	90.3	23	9.7	
No School-Age or Prior ADHD	218	199	91.3	19	8.7	
		No Antidepressants		Antidepressants		
	Total N	N %		N	%	
No School-Age MDD or Anxiety	152	151	99.3	1	0.7	
No School-Age or Prior MDD or Anxiety	115	115	100.0	0	0.0	
		No ADHD Meds		ADHD Meds		
	Total N	Ν	%	N	%	
No Adolescent/Early Adult ADHD	170	146	85.9	24	14.1	
No Adolescent/Early Adult or Prior ADHD	129	117	90.7	12	9.3	
		No Antidepressants		Antidepressants		
	Total N	N	%	Ν	%	
No Adolescent/Early Adult MDD or Anxiety	92	87	94.6	5	5.4	
No Adolescent/Early Adult or Prior MDD or Anxiety	42	41	97.6	1	2.4	

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, MDD = major depressive disorder.

Supplementary Table 6. ADHD severity scores in children without a research diagnosis of ADHD by ADHD medication prescription status

	No Preschool ADHD;			No P	reschool A	No ADHD Meds		
	No Preschool ADHD Meds		Presch	nool ADHD	vs. ADHD Meds			
	Ν	Mean	SD	Ν	Mean	SD	t	р
ADHD severity	237	3.00	3.02	7	4.86	2.54	-1.61	0.1090
	No School-Age ADHD; No School-Age ADHD;			ADHD;				
	No School-Age ADHD Meds			School	-Age ADHI			
	Ν	Mean	SD	Ν	Mean	SD	t	Р
ADHD severity	214	2.19	2.37	23	5.35	3.04	-5.90	<0.0001
	No Adolescent/Early Adult ADHD; No Adolescent/Early Adult		No Adolescent/Early Adult ADHD; Adolescent/Early Adult					
	N	Mean	SD	, N	Mean	SD	t	Р
ADHD severity	59 ^a	0.49	1.18	8	2.75	2.19	-2.86	0.0223

*Differences were considered significant if p < 0.05 (shown in bold).

^aADHD scores not available for all adolescent participants due to the format of the K-SADS.

Abbreviations: SD = standard deviation, ADHD = attention-deficit/hyperactivity disorder, K-SADS = Kiddie-

Schedule for Affective Disorders and Schizophrenia.

Supplementary Figure 1. Generalized Estimating Equations of Psychotropic Medication Prescription by Age and Time-Varying PECFAS/CAFAS Score or Diagnosis Severity Score Covarying for Sex and Time-Varying Income-to-Needs Ratio



Footnote: X-axis = age; Y-axis = probability of medication use; Blue line = mean -1 SD value of independent variable; Red line = mean value of independent variable; Green line = mean +1 SD value of independent variable. The main effect of the independent variable was significant at p<0.0001 for all models.

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, MDD = major depressive disorder, ODD = oppositional defiant disorder, CD = conduct disorder, PECFAS = Preschool and Early Childhood Functional Assessment Scale, CAFAS = Child and Adolescent Functional Assessment Scale, SD = standard deviation.