Adolescent Antidepressant Use and Academic Achievement

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Motivation: prevalence of mental health disorders

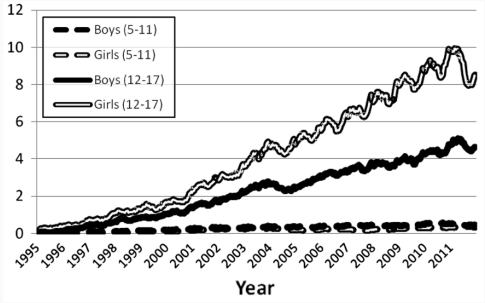
- Mental health disorders (MHD) affect 11% of the world population
- They account for 10% of years lived with disability
- Growing disease burden: by 2030, depression alone is predicted to become the leading cause of disability in high-income countries
- **Most mental health disorders emerge during childhood** (Kessler et al., 2007)
  - US (age 3–17): 7.1% anxiety, 3.2% depression, 7.4% behavioral problems (CDC)
  - Denmark (up to age 18): 6.1% anxiety, 1.64% depression, 1.68% eating and personality disorders (Dalsgaard et al., 2020)

Motivation: the treatment gap

- **Large treatment gaps**: estimated at 60% (Kohn et al., 2004)
- Treating MHDs could potentially bring health and economic gains
- Given negative selection into MHDs and positive selection into treatment, increasing access to treatment could also lower health and economic inequality
- Early intervention is important: most MHDs have inbuilt persistence so the gains from treatment could be greater if they are introduced early in life

Motivation: pharmaceutical treatment of MHDs

- Antidepressants are the first line of treatment for MHD among youth
- Strong trend in use, not driven by increased diagnosis (Pottegård et al., 2014)



Denmark: Number of 5–17 yeard olds with SSRI prescription per 1,000 children (Pottegård et al., 2014)

What we do

- Investigate impacts of antidepressant treatment on test scores at age 16
- Danish administrative data on children who had contact with a private child psychiatrist during ages 8-15
- Address selection into receiving antidepressant treatment by leveraging plausibly exogenous variation in the prescribing tendency of psychiatrists
  - similar to other studies using quasi-random assignment of cases to decision makers (mostly judges) (Kling, 2006; Doyle, 2007; Maestas et al., 2013; Dahl et al., 2014; Aizer and Doyle, 2015; Bhuller et al., 2018;)
- Estimate marginal treatment effects (MTE) to explore heterogeneity in the LATE

What we find

- SSRI treatment increases test scores; estimates larger and only significant for Math
- Estimates larger and only significant for girls
- The slope of the MTE curve reveals that SSRI treatment increases test scores most for children whose unobservables render them likely to take up SSRI regardless of the prescribing tendency of the physician
- MTEs are positive except at the very top of the distribution of unobserved resistance to treatment

Related Research

- Previous work on depression and school performance
  - Depression raises school dropout and lowers GPA, especially for girls, identified with sibling FE (Fletcher 2008, 2010), individual FE (Eisenberg et al., 2009), and genetic markers as instruments (Ding et al., 2009)
  - Anti-anxiety app raises performance on a cognitive task (Cavatorta et al., 2020)
  - **Only one study of antidepressants and GPA:** 2004 FDA warning reduced antidepressant use and led to lower test scores among adolescents with probable depression (Busch et al., 2014)
- Previous work on treatment of depression and economic activity
  - Treating depression increases labour supply (Lund et al., 2019 provide a meta-analysis of 36 RCTs in developing countries) and control over household income (Baranov et al., 2020)
  - 2007 FDA warning lowered female employment (Butikofer et al., 2020)

Contributions

- Provide the first evidence on the causal effect of antidepressant use on cognition
  - contribute to evidence that treating MHDs has an economic payoff
  - results speak to controversy on over- vs under-use of antidepressants among children
- Shed light on mechanisms because our results are consistent with evidence that:
  - attention deficits have a larger impact on math than on language performance (Marie and Zolitz, 2017)
  - girls are more sensitive to attention deficits (Marie and Zolitz, 2017; Cavatorta et al., 2020)
- Implicitly provide evidence that interventions beyond early childhood have long-run effects (Hendren and Sprung-Keyser, 2020)

Diagnosis and treatment of mental health disorders

- In Denmark, non-elective health care is free of charge for all residents
- GPs act as a gatekeeper for specialist care
- The Danish Health and Medicines Authority exclusively delegates diagnosis and treatment of MHDs among children and adolescents to specialists
  - private child psychiatry practices
  - hospital psychiatric departments
- Severe cases are generally assigned to hospitals
- Initial treatment includes non-pharmacological interventions such as psychotherapy and this may continue alongside antidepressants
- If a pharmacological treatment is prescribed, prescription drug costs are subsidized

Data and analysis sample

- All native children born between 1989–1999
- Define a newly diagnosed mental health disorder as:
  - no contact with a child psychiatrist at ages 6–7
  - contact with a child psychiatrist between ages 8–15
- Among 8–15 year olds, the share with a new MH diagnosis is 5.4%
- 15% of these children are diagnosed by a private psychiatrist, the rest by a hospital psychiatric department
- We focus on 4,940 children diagnosed in 21 private child psychiatry practices (hospitals take more severe cases and we do not observe the diagnosing physician)
  - median age at diagnosis is 11.6
  - 18% fill an SSRI prescription between ages 8–15
  - median age at first SSRI prescription is 13
  - median duration between diagnosis and first SSRI prescription is 61 days

Empirical strategy

- Our main equation of interest is:

$$Y_i = \beta_0 + AD_i\beta_1 + \mathbf{X}_i\beta_2 + \gamma_b + \alpha_t + m_i + \epsilon_i$$

  where the unit of observation is child i
  - Y_i is a standardized test score in 9th grade
  - AD_i is an indicator for SSRI use
  - $\mathbf{X}_i$ is a vector of observable characteristics measured at baseline (when the child is 6)
  - γ_b, α_t, and m_i are year-of-birth, year-of-diagnosis, and municipality-of-residence fixed effects
- Standard errors are clustered at the specialist and year-of-diagnosis level
- The parameter of interest β_1 captures the average effect of SSRI use on academic achievement

Instrument: prescribing tendency of physician

- Exploit “random" assignment of children to psychiatrists: limited number of specialists constrain parental choice of providers (31 child psychiatry units in 2003)
- Instrument for child i is the fraction of other 8–15 year old children who obtain SSRI from the same specialist k in the year of the first MH visit of child i:

$$PP_i^k = \frac{\sum_{j \neq i} AD_j^k}{N^k}$$

- Assignment to the first specialist averts endogenous provider changes
- Data span 15 years so we calculate the instrument at the physician-year level, allowing learning or other changes in specialist preferences over time (Mueller-Smith, 2015)
- If the 2SLS assumptions are satisfied, the 2SLS estimand represents the weighted average of the causal effect of SSRI treatment among those who would not have received pharmacological treatment had they first seen a different psychiatrist

Instrument validity: relevance

- A psychiatrist's prescribing tendency should have a strong effect on the patient's probability of receiving SSRI treatment
- There tends to be a lot of physician-level variance in treatment choices across conditions (Finkelstein et al., 2015, 2017; Cutler et al., 2019), possibly more so for MHDs where there is greater uncertainty over the right choice (Berndt et al., 2015; Currie and McLeod, 2020; Marquardt, 2021)
- The instrument has sufficient power in our setting
- We nevertheless show CIs that account for weak instruments (Andrews, 2018)

Instrument validity: conditional independence

- A specialist's propensity to prescribe SSRI should not be correlated with (observable and unobservable) characteristics of the child and their family
- Scope for endogenous choice of initial provider is limited so we assign patients to the first provider they visit
- In the spirit of balancing tests, we show that the instrument is uncorrelated with a rich set of observable characteristics that predict academic performance

Instrument validity: exclusion restriction

- A specialist's prescribing tendency should affect academic achievement only through its effect on the probability that the child uses SSRIs
- A key concern is if high SSRI prescribing physicians are also better at providing other treatments that impact academic achievement
- The fragmented health care system in DK alleviates such concerns
- We also show that the likelihood of receiving non-pharmacological treatments after diagnosis is balanced across the distribution of the instrument

Instrument validity: monotonicity

- Children who are prescribed SSRI by a low-prescribing specialist would also receive SSRI treatment from a high-prescribing specialist (and vice versa)
- Check the first-stage results in different subsamples
- Redefine the instrument in a given subsample to be the psychiatrist's prescribing tendency for patients outside of the subsample (e.g., when focusing on girls, the instrument is defined for boys) and estimate the first-stage with "reverse-sample instrument"

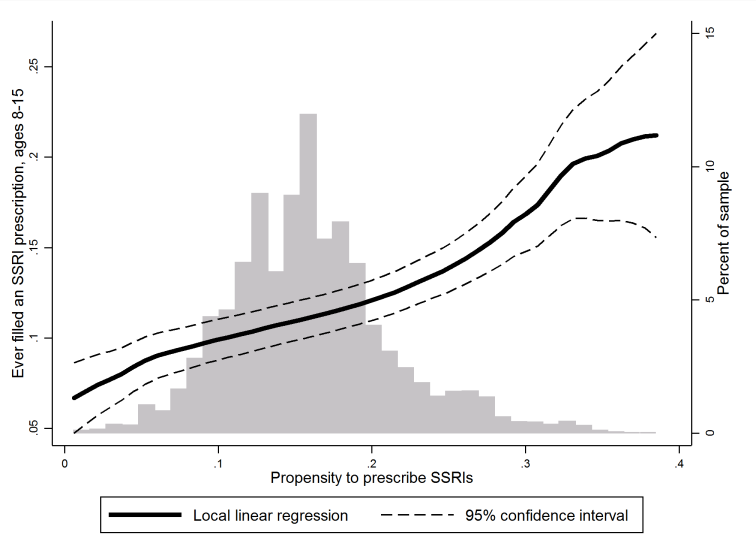
Descriptive statistics

	No psychiatric contact (1)	Analysis sample All (2)	No SSRI (3)	SSRI (4)	*p*-value (5)
A. Outcomes					
Standardized test score, math	0.073	−0.235	−0.249	−0.172	0.070*
	(0.973)	(1.018)	(1.025)	(0.983)	
Standardized test score, Danish	0.059	−0.140	−0.184	0.056	0.000***
	(0.986)	(1.017)	(1.013)	(1.013)	
B. Child characteristics					
Boy	0.506	0.613	0.637	0.506	0.000***
First born	0.440	0.480	0.485	0.458	0.135
Parents are married	0.806	0.672	0.653	0.756	0.000***
Had therapy provided by GP or psychologist before first MH visit	—	0.155	0.125	0.289	0.000***
C. Clinic characteristics					
Number of patients treated by specialist during year	—	149.527	149.553	149.414	0.959
		(74.248)	(74.383)	(73.681)	
Propensity to prescribe SSRIs	—	0.122	0.118	0.142	0.000***
		(0.065)	(0.063)	(0.067)	
Had therapy provided by GP or psychologist after first MH visit	—	0.091	0.072	0.175	0.000***
Observations	589,023	4,940	4,036	904	

Descriptive statistics

	No psychiatric	Analysis sample			
	contact	All	No SSRI	SSRI	*p*-value
	(1)	(2)	(3)	(4)	(5)
D. Mother's characteristics at child age 6					
Age	35.254	35.127	34.984	35.764	0.000***
	(4.623)	(4.950)	(4.974)	(4.791)	
Years of education	13.600	13.459	13.385	13.791	0.000***
	(2.259)	(2.380)	(2.384)	(2.332)	
Employed	0.834	0.774	0.768	0.801	0.025**
Annual gross total income (thousands 2015 DKK)	311.193	311.125	311.050	311.456	0.925
	(196.587)	(124.427)	(126.250)	(116.007)	
E. Father's characteristics at child age 6					
Age	37.752	37.633	37.476	38.333	0.000***
	(5.465)	(5.747)	(5.715)	(5.839)	
Years of education	13.728	13.610	13.569	13.793	0.016**
	(2.425)	(2.566)	(2.579)	(2.502)	
Employed	0.931	0.892	0.888	0.907	0.083*
Annual gross total income (thousands 2015 DKK)	425.222	415.429	414.591	419.173	0.636
	(453.332)	(300.136)	(310.067)	(251.169)	
Observations	589,023	4,940	4,036	904	

First-stage is well-behaved and fairly strong



First-stage coefficient: 0.760 (0.122)
F-statistic: 39.010
An interquartile shift in the distribution of propensity to prescribe increases probability of SSRI by 6 percentage points

Cannot reject instrument exogeneity

	SSRI use (1)	Specialist propensity to prescribe SSRI (2)
Boy	−0.076***	−0.003*
	(0.012)	(0.002)
Married parents	0.043***	0.001
	(0.012)	(0.002)
Mother's age	0.002	0.000
	(0.001)	(0.000)
Mother's years of education	0.009***	−0.000
	(0.003)	(0.000)
Mother employed	0.005	0.002
	(0.017)	(0.002)
Father's age	0.002	−0.000
	(0.001)	(0.000)
Father's years of education	−0.000	−0.001
	(0.002)	(0.000)
Father employed	−0.002	0.004
	(0.022)	(0.003)
Observations	4,915	4,915

Regressions also include indicators for birth order, family size, and deciles of parental income, and the fixed effects in baseline specification.

Cannot reject instrument exogeneity

	Predicted standardized test score	
	Math	Danish
	(1)	(2)
Specialist propensity to prescribe	−0.061	0.072
	(0.165)	(0.113)
Effect of interquartile shift in instrument	−0.005	0.006
Mean outcome	0.016	−0.030
Observations	4,915	4,915

Regressions also control for year-of-diagnosis and municipality-of-residence fixed effects.

Cannot reject instrument monotonicity

	Quartile of predicted outcome			
	First	Second	Third	Fourth
	(1)	(2)	(3)	(4)
Standardized test score, math	0.680***	0.837***	0.704***	0.701***
	(0.192)	(0.185)	(0.250)	(0.249)
Effect of interquartile shift in instrument	0.054	0.067	0.056	0.056
Observations	1,231	1,228	1,229	1,227
Standardized test score, Danish	0.806***	0.662***	0.773***	0.804***
	(0.165)	(0.185)	(0.270)	(0.286)
Effect of interquartile shift in instrument	0.064	0.053	0.062	0.064
Observations	1,231	1,230	1,229	1,225

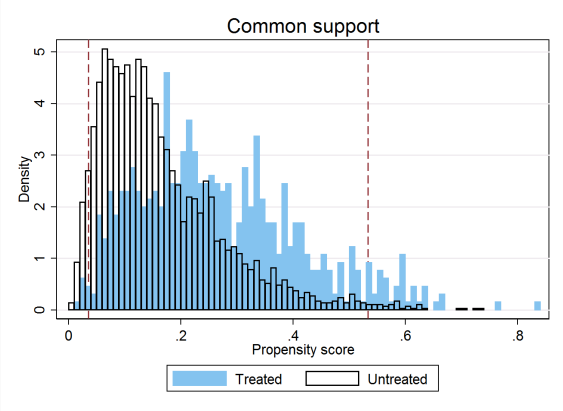
Cannot reject instrument monotonicity

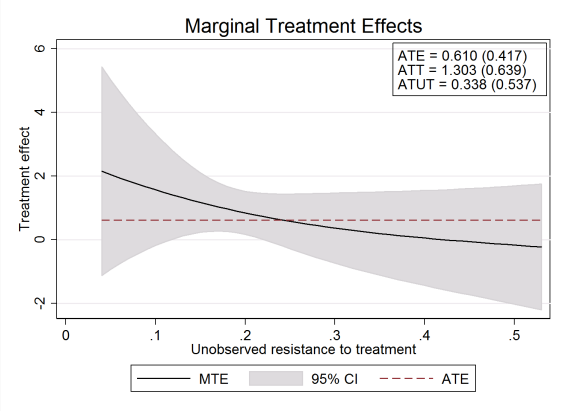
	Gender		Mother's years of education	
	Boy	Girl	At least 13	Less than 13
	(1)	(2)	(3)	(4)
Specialist propensity to prescribe	0.428***	0.933***	0.887***	0.844***
	(0.102)	(0.230)	(0.124)	(0.205)
Mean outcome	0.148	0.227	0.190	0.157
Observations	2,143	1,487	2,618	1,012
First-stage F statistic	17.462	16.476	51.307	16.938
Effect of interquartile change in instrument	0.058	0.062	0.083	0.074

Baseline results: Math scores improve 0.86SD, no discernible impact on Danish

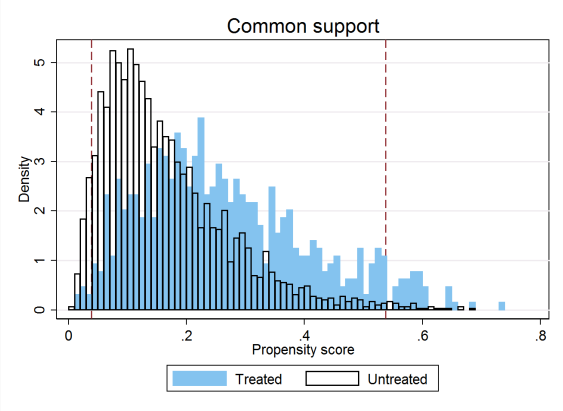
	OLS	Reduced form	IV
	(1)	(2)	(3)
Math	0.058	0.652**	0.858**
(Mean $= -0.247, N = 3,630$)	(0.046)	(0.271)	(0.385)
Weak-instrument-robust 95% CI			$[0.225, 1.715]$
Wild bootstrap p-value			0.032
Effect of interquartile shift in instrument		0.052	
Danish	0.150***	0.135	0.180
(Mean $= -0.186, N = 3,576$)	(0.042)	(0.240)	(0.323)
Weak-instrument-robust 95% CI			$[-0.414, .837]$
Wild bootstrap p-value			0.533
Effect of interquartile shift in instrument		0.011	

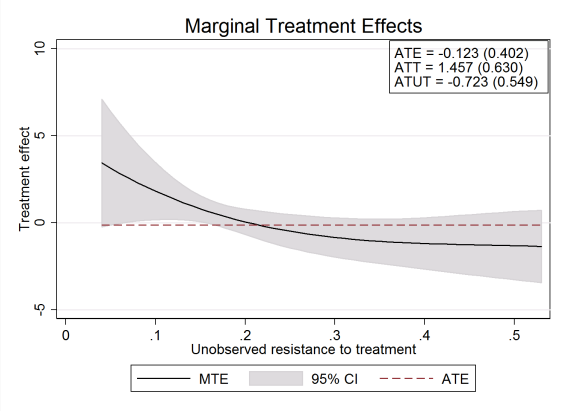
Marginal treatment effects, Math: positive almost everywhere





Marginal treatment effects, Danish: positive only at low unobserved resistance





Math scores improve 0.99SD for girls, smaller and not significant for boys

	OLS	First stage	Reduced form	IV
	(1)	(2)	(3)	(4)
Girls	0.056	0.823***	0.811**	0.985*
(Mean $= -0.295$, $N = 1,487$, First-stage $F = 23.235$)	(0.061)	(0.171)	(0.400)	(0.521)
Weak-instrument-robust 95% CI				[0.152, 2.113]
Wild bootstrap p-value				0.062
Effect of interquartile shift in instrument		0.066	0.065	
Boys	0.051	0.691***	0.462	0.669
(Mean $= -0.217$, $N = 2,143$, First-stage $F = 18.112$)	(0.060)	(0.162)	(0.368)	(0.539)
Weak-instrument-robust 95% CI				[−0.309, 1.854]
Wild bootstrap p-value				0.236
Effect of interquartile shift in instrument		0.055	0.037	

Danish scores do not improve for boys or girls

	OLS	First stage	Reduced form	IV
	(1)	(2)	(3)	(4)
Girls	0.062	0.819***	0.152	0.186
(Mean $= 0.165, N = 1,505$, First-stage $F = 24.029$)	(0.056)	(0.167)	(0.411)	(0.500)
Weak-instrument-robust 95% CI				$[-0.804, 1.175]$
Wild bootstrap p-value				0.733
Effect of interquartile shift in instrument		0.065	0.012	
Boys	0.216***	0.638***	−0.052	−0.081
(Mean $= -0.417, N = 2,071$, First-stage $F = 14.552$)	(0.064)	(0.167)	(0.395)	(0.616)
Weak-instrument-robust 95% CI				$[-1.316, 1.272]$
Wild bootstrap p-value				0.898
Effect of interquartile shift in instrument		0.051	−0.004	

Conclusions

- Among 16 year olds diagnosed with MH disorders, Math test scores are 0.86 SD higher among those on SSRI
- Estimates 30% larger and only significant among girls
  - girls are more likely to have MH disorders, have more severe problems (pre-diagnosis therapy: 20% girls vs 12% boys), and are more likely to be prescribed SSRIs
  - evidence suggests that test scores are more elastic to inputs for girls than for boys
- Stronger effects for girls and math implies SSRIs improving attention deficit problems as a plausible mechanism
- Concentration of effects on girls x math suggests that MHDs contribute to under-performance & under-enrollment of girls in STEM subjects
- Our results indicate large detrimental impacts of mental health disorders on cognitive performance, and high returns to antidepressant treatment

Next steps

- Conduct additional robustness checks (age range, treatment definition, clustering etc.)
- Add new outcome variables (test taking behavior, education beyond compulsory schooling, suicide attempts, ER visits, etc.)
- Explore effects along the distribution of test scores (quantile IV)
- Investigate OLS vs IV differences: selection or treatment heterogeneity?
- Explore treatment heterogeneity by other observable characteristics

Descriptive statistics by type of first mental health contact

	No psychiatric contact (1)	Hospital contact (2)	Analysis sample (3)
A. Child characteristics			
Boy	0.506	0.581	0.613
First born	0.440	0.454	0.480
Parents are married	0.806	0.647	0.672
Median age at first MH visit	—	12.417	11.583
B. Mother's characteristics at child age 6			
Age	35.254	34.544	35.127
	(4.623)	(5.034)	(4.950)
Years of education	13.600	12.969	13.459
	(2.259)	(2.259)	(2.380)
Employed	0.834	0.729	0.774
Annual gross total income (thousands 2015 DKK)	311.193	291.915	311.125
	(196.587)	(109.530)	(124.427)
C. Father's characteristics at child age 6			
Age	37.752	37.270	37.633
	(5.465)	(5.839)	(5.747)
Years of education	13.728	13.134	13.610
	(2.425)	(2.452)	(2.566)
Employed	0.931	0.870	0.892
Annual gross total income (thousands 2015 DKK)	425.222	375.736	415.429
	(453.332)	(230.542)	(300.136)
Observations	589,023	28,573	4,940

Descriptive statistics by type of first mental health contact

	No psychiatric contact (1)	Hospital contact (2)	Analysis sample (3)
D. Treatments, age 8–15			
Ever filled an SSRI prescription	0.001	0.115	0.183
Median age at first SSRI prescription	14.250	13.667	13.083
Median days between first MH visit and first SSRI prescription	—	112	61
Had therapy provided by GP or psychologist after first MH visit	—	0.090	0.091
E. Guidelines violations			
Filled SSRI prescription before first MH visit	—	0.020	0.025
Ever filled a tricyclic antidepressant prescription, age 8–15	0.001	0.003	0.002
Ever filled a benzodiazepine prescription, age 8–15	0.006	0.029	0.021
F. Clinic characteristics			
Transfer between private clinic and hospital	—	0.026	0.164
Number of patients treated during year	—	899.688	149.527
		(841.503)	(74.248)
Propensity to prescribe SSRIs	—	0.117	0.122
		(0.055)	(0.065)
Observations	589,023	28,573	4,940