NEW RESEARCH

Effect of Pharmacological Treatment of Attention-Deficit/Hyperactivity Disorder on Criminality

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Objective: Criminality rates are higher among persons with attention-deficit/hyperactivity disorder (ADHD), and evidence that medication reduces crime is limited. Medication rates between clinics vary widely even within universal health care systems, partly because of providers' treatment preferences. We used this variation to estimate causal effects of pharmacological treatment of ADHD on 4-year criminal outcomes.

Method: We used Norwegian population-level registry data to identify all unique patients aged 10 to 18 years diagnosed with ADHD between 2009 and 2011 (n = 5,624), their use of ADHD medication, and subsequent criminal charges. An instrumental variable design, exploiting variation in provider preference for ADHD medication between clinics, was used to identify causal effects of ADHD medication on crime among patients on the margin of treatment, that is, patients who receive treatment because of their provider's preference.

Results: Criminality was higher in patients with ADHD relative to the general population. Medication preference varied between clinics and strongly affected patients' treatment. Instrumental variable analyses supported a protective effect of pharmacological treatment on violence-related and public-order–related charges with numbers needed to treat of 14 and 8, respectively. There was no evidence for effects on drug-, traffic-, sexual-, or property-related charges.

Conclusion: This is the first study to demonstrate causal effects of pharmacological treatment of ADHD on some types of crimes in a population-based natural experiment. Pharmacological treatment of ADHD reduced crime related to impulsive-reactive behavior in patients with ADHD on the margin of treatment. No effects were found on crimes requiring criminal intent, conspiracy, and planning.

Study preregistration information: The ADHD controversy project: Long-term effects of ADHD medication; https://www.isrctn.com/; 11891971.

Key words: ADHD; pharmacological treatment; quasi-experiment

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Attention-deficit/hyperactivity disorder (ADHD) is associated with criminality.[1-5] Although the prevalence of ADHD is estimated to be 5.9% in youth and 2.5% in adults,[6] it is 25% among prisoners.[7] Potential mechanisms for this over-representation include increased risky behavior among persons with ADHD,[8] and exposure to compounding family risks and deviant peers.[1,9] Early detection and appropriate treatment is called for to prevent crime and to reduce social costs in this patient group.[6,10,11]

Pharmacological treatment of ADHD is common,[6] and randomized controlled trials (RCTs) show reduced short-term symptoms, although evidence of effectiveness on funtional outcomes such as crime remains uncertain.[12] A systematic review of research on ADHD and crime concludes that knowledge about treatment effects on crime is limited and that small samples in past research may contribute to inconclusive findings.[1,13] A comprehensive RCT found no crime protective effects of ADHD medication relative to other treatments after 8 years.[14] Scandinavian registry-based within-subjects studies comparing crime in periods on and off medication report mixed results, including reductions in violence-, drug-, and traffic-related crimes[2,15] or no reduction.[16] Notably, within-subjects designs cannot rule out all unmeasured confounding, such as time-varying symptom severity, that may affect both

treatment and criminality.[17] Overall, the question of whether pharmacological treatment of ADHD reduces crime remains unanswered.

This study estimates causal effects of pharmacological treatment of ADHD on crime using a quasi-experimental, provider-preference–based instrumental variables (IV) design. Our approach circumvents unmeasured confounding that may otherwise bias treatment effects, as symptom severity is positively associated with crime[18] and pharmacological treatment. IV mimics RCTs by exploiting a source of "as good as" random variation in treatment instead of investigator-led randomization. We use variation in provider preference for pharmacological treatment as an IV.[19] Patients with moderate symptom severity may receive pharmacological treatment in one clinic but not another, and patients cannot choose providers based on desired outcomes in our institutional setting (ie, the Norwegian universal health care system), as their provider is assigned by residence municipality. Our IV analysis estimates the average treatment effect of pharmacological treatment of ADHD for patients "on the margin of treatment," that is, patients who would vs would not receive treatment depending on their provider's medication preference. Thus, the estimate may not generalize to patients who would receive medication regardless of which provider they attend.

The main aim of this study is to estimate the effect of pharmacological treatment of ADHD on crime for patients on the margin of treatment. We also provide population-based evidence on rates of crime in ADHD compared to that in the general population.

METHOD

Sample

Our patient sample includes all individuals born between 1991 and 2001 who received their first ADHD diagnosis from the Norwegian Child and Adolescent Mental Health Services (CAMHS) between 2009 and 2011 (ages 10-18), as registered in the Norwegian Patient Registry (N = 5,624). ADHD diagnoses are defined as all *International Classification of Diseases, Tenth Revision* (*ICD-10*) hyperkinetic disorder codes, namely F90.0 (80.5%), F90.1 (11.0%), F90.8 (7.4%), and F90.9 (1.1%). *ICD-10* hyperkinetic disorder corresponds mainly to *DSM-IV* ADHD combined type and *DSM-V* ADHD combined clinical presentation.[20] In *ICD-10,* co-occurring hyperkinetic disorder and oppositional defiant disorder (ODD) or conduct disorder (CD) is coded as F90.1 hyperkinetic conduct disorder. Younger birth cohorts (2002-2006) were excluded, as they had a very low risk of crime during follow-up (Figure S1, available online). We also analyze a general population sample comprising a random sample of persons 10 to 18 years of age without contact with CAMHS in 2009 to 2011 matched on age, sex, and geography, given a random inclusion date instead of date of diagnosis in 2009 to 2011 (N = 50,271).

Criminal Charges

Crime was measured by using all criminal charges that resulted in a prosecutor's decision to indict, fine, conditionally discharge, dismiss on grounds of not being criminally responsible (eg, because of mental illness or age), or refer to juvenile mediation, as registered in the Central Penal and Police Registry (see criminal charges by decision, Table S1, available online, and clearance rate for crimes, Table S2, available online).

We defined a global crime indicator as having been charged for any of the 7 Statistics Norway crime categories: property theft, violence and abuse (henceforth violence), sexual, drug, public order, and integrity violations (henceforth public order), traffic, and other. "Other" included property damage, other crimes (eg, environmental), and other crimes of acquisition (eg, deception). Persons of all ages can be charged for crimes, although the minimum age is 15 for criminal prosecution.[21] We coded cumulative binary indicators taking value 1 for 1 or more charges and 0 otherwise for each year of follow-up.

ADHD Medication

We used all filled prescriptions in the Norwegian Prescription Database for ADHD medication as defined by the Norwegian Institute of Public Health (percentage of total ADHD prescriptions over follow-up in parentheses). Stimulants included methylphenidate (N06BA04, 89.8%), dexamphetamine (N06BA02, 0.6%), lisdexamfetamine (N06BA12, 0.06%), and amphetamine (N06BA01, 0.06%). Non-stimulants included atomoxetine (N06BA09, 9.5%). Pharmacological treatment is defined as the cumulative number of daily defined doses (DDD) filled for any ADHD prescriptions over the years following an ADHD diagnosis. For ease of interpretation, the treatment variable was scaled so that a 1-unit increase in the treatment variable represented an increase from 0 to full-time medication in the entire follow-up period. For example, pharmacological treatment for the first year of follow-up was measured as the cumulative number of DDD for ADHD prescriptions divided by 365. Hence, the treatment variable equaled 1 if the patient filled prescriptions corresponding to 365 days of pharmacological treatment.

Covariates

We used patient, family, and clinic area covariates to adjust for patient mix (for overview of data sources, see Table S3,

available online). Patient and family covariates were measured prior to or at the time of ADHD diagnosis, whereas catchment area characteristics were measured during 2009 to 2011 to prevent post-treatment bias. We included: age, sex, year of contact with clinic, psychiatric comorbidity at time of diagnosis, country of birth (Norway, Europe, outside of Europe), charges before ADHD diagnosis, parents' marital status (married, unmarried, other [widowed, divorced, separated]), parent's highest education when the child was 6 years of age (primary school, high school, short and long university education), and parent's labor income when the child was 6 years of age. Covariates on catchment area characteristics were included to account for potential area-level common causes of provider preference and crime. We included municipality-level population size and high school dropout rates, and the following aggregated measures from the random sample of the general population: municipality-level labor income of parents and clinic-level percentage of youth crime, youth immigrants, mothers' marriage rate, and parents' education level.

Statistical Analyses

Risk ratios for any crime and types of crimes at 8-year follow-up for patients with ADHD relative to the matched sample were calculated using generalized linear models with the binomial family and log link-function. Models were stratified by sex and were age adjusted.

Linear probability models (LPMs) were used to estimate associations between pharmacological treatment and criminal charges.[22] Analyses were conducted on multiple samples: all patients, all patients excluding F90.1, that is, patients with additional behavioral challenges, stratified by sex because of potentially important differences in ADHD and criminality, by stimulants/non-stimulants (as effectiveness may differ), and patients 14 to 18 years at the time of diagnosis. Analyses were also conducted using Probit models as robustness checks. Causal interpretation of LPM estimates requires that the exposure is assumed to be conditionally random given covariates.[23] This is unlikely and motivates our IV design. LPM models are nonetheless included for comparison purposes to IV results, in line with the common convention in IV analysis.[19,24]

The IV design used the observed variation in pharmacological treatment between clinics as quasi-randomization to pharmacological treatment accounting for patient mix. In Norway, only psychiatrists are licensed to initiate pharmacological treatment, but they work in teams with other professions. Broadly, provider preferences are measured as the clinic-level average number of DDDs for filled ADHD prescriptions among patients with ADHD, cumulatively and separately for 1 to 4 years. Four years were chosen for IV analysis, as the IV was sufficiently strong for this duration only. Specifically, the leave-one-out average was used to measure provider preference for all patients other than patient *i*, thereby eliminating potential influence of patient *i* on the provider preference relevant to him or her. For ease of interpretation, IVs are scaled the same way as treatment. IV analyses are conducted for the same samples as LPMs. The estimand is the local average treatment effect (LATE), that is, the average causal effect of pharmacological treatment for patients on the margin of pharmacological treatment.[22]

A valid provider preference IV requires the following assumptions (see Supplement 1 for details, available online): relevance, exclusion, independence, monotonicity, and the stable unit treatment value assumption.[22] Relevance is empirically tested with the IV's F statistic in first-stage regressions of treatment on IV and covariates. Exclusion is evaluated by reduced form estimates in the general population sample where provider preference should not affect crime. Independence is tested by examining covariate balance for the IV. Monotonicity is tested by examining residuals from first-stage regressions against values of the IV. The LATE was estimated with 2-stage least squares (2SLS) and, as robustness checks, IV Probit models.[25] All models clustered standard errors at the clinic level and were conducted in Stata 17,[26] using coefplot for data visualization.[27] Reporting guidelines for IV analysis[28] were followed, and hypotheses were pre-registered (ISRCTN: 11891971) and protocolled.[29]

RESULTS

Descriptive Statistics

Table 1 shows baseline characteristics of the ADHD patient sample and the matched general population sample. The ADHD sample was somewhat younger, with more male persons, persons of Norwegian background, and criminal charges before inclusion. Parents of patients with ADHD had lower income, education, and were less likely to be married. Catchment area characteristics were relatively similar. Table 2 shows considerably higher rates of charges among patients with ADHD compared to the matched general population, and large sex differences, over 8-year follow-up. The highest risk ratios were for violence-related and sex-related charges. Risk ratios were relatively similar by 4-year follow-up (Tables S4 and S5, available online).

Assessment of the Instrumental Variable

Overall, 79% of all patients had filled $\geq$1 ADHD prescription during the first year after diagnosis, whereas 87% had filled $\geq$1 prescription by 4 years. The average percentage of patients who had filled $\geq$1 ADHD prescription varied from 42% to 100% between clinics by 4-year

TABLE 1 Baseline Characteristics for Patients With ADHD and the General Population, 10 to 18 Years of Age in 2009 to 2011 (N = 55,896)

Characteristics	ADHD diagnosis (n = 5,624)		General population (n = 50,271)	
Individual characteristics				
Age at diagnosis, mean ± SD[a]	13.5	± 2.5	14.0	± 2.6
Male persons, n (%)	3,714	(66.0)	24,705	(51.1)
Country of birth, n (%)				
Norway	4,405	(78.3)	35,601	(70.8)
Europe	767	(13.6)	7,340	(14.6)
Outside of Europe	452	(8.0)	7,330	(14.6)
Crime before diagnosis, n (%)	417	(7.4)	888	(1.8)
Psychiatric comorbidity, n (%)	1,515	(27.0)	-	-
Family characteristics				
Parents' labor income (USD), mean ± SD[b]				
Labor income, father	49,746	± 36,020	60,496	± 55,342
Labor income, mother	24,912	± 22,150	29,658	± 24,432
Parents' highest education, n (%)				
University long, father	213	(3.8)	4,856	(9.7)
University short, father	644	(11.5)	9,855	(19.6)
High school, father	2,699	(48.0)	22,753	(45.3)
Primary school, father	1,827	(32.5)	9,812	(19.5)
University long, mother	119	(2.1)	2,837	(5.6)
University short, mother	1,062	(18.9)	14,304	(28.5)
High school, mother	2,449	(43.6)	19,732	(39.3)
Primary school, mother	1,900	(33.8)	10,916	(21.7)
Parents' civil status, n (%)				
Unmarried, father	1,412	(25.5)	8,463	(16.8)
Married, father	2,698	(48.0)	31,252	(62.2)
Other, father	1,154	(20.5)	7,112	(14.2)
Unmarried, mother	1,560	(27.7)	9,155	(18.2)
Married, mother	2,706	(48.1)	31,242	(62.2)
Other, mother	1,248	(22.2)	7,824	(15.6)
Catchment area characteristics				
Youth crime (≥1 charge), % ± SD	3.0	± 0.7	3.0	± 0.7
Youth immigrants, % ± SD	24.9	± 10.6	27.8	± 13.0
Parents' primary school education, % ± SD	8.0	± 4.7	8.8	± 5.9
Parents' married, % ± SD	61.5	± 6.4	62.9	± 6.3
Parents' labor income (USD), mean ± SD	50,663	± 8,527	52,375	± 11,337
High school dropout, % ± SD	25.6	± 5.1	24.9	± 5.5
Population (0-65+ y), mean ± SD	33,060	± 38,126	36,600	± 38,413

Note: ADHD diagnosis when in contact with CAMHS 2009 to 11, and matched general population excluding those in contact with CAMHS 2009 to 11. ADHD = attention-deficit/hyperactivity disorder; CAMHS = child and adolescent mental health services; n = number; NOK = Norwegian kroner; SD = standard deviation; USD = US dollar; yrs = years.

[a]*Plus-or-minus values are mean ± SD. Age at diagnosis corresponds to age at inclusion for the general population.*

[b]*Yearly with USD/NOK exchange rate average for 2010 (USD 1/NOK 6.0453).*

follow-up (Figure S2, available online). Clinics had a median of 52 patients (interquartile range [IQR]: 66) who were diagnosed with ADHD in 2009 to 2011.

Figure 1A shows the distribution of provider preference for ADHD medication. The median provider preference decreased from prescribing 0.72 DDD (IQR: 0.24) over the first year of follow-up to 0.64 DDD (IQR: 12). The relationship between treatment values and provider preference were positively increasing, lending support to monotonicity (Figure S3, available online).

Figure 1B further shows that the largest variation in provider preference occurs in the first year, followed by a

TABLE 2 Persons With ADHD, General Population, and Risk of Criminal Charges Over 8-Year Follow-up After 2009 to 2011 (N = 54,198)

Crime	ADHD diagnosis, n (%)			Matched general population, n (%)			Risk ratios comparing ADHD to general population					
	Male persons	Female persons	Total persons	Male persons	Female persons	Total persons	Male persons		Female persons		Total persons	
	(n = 3,664)	(n = 1,867)	(n = 5,531)	(n = 24,994)	(n = 23,673)	(n = 48,667)	RR	95% CI	RR	95% CI	RR	95% CI
Any crime	1,410 (38.48)	343 (18.37)	1,753 (31.69)	4,714 (18.86)	1,300 (5.49)	6,014 (12.36)	2.28	[2.18, 2.39]	3.35	[3.00, 3.73]	2.71	[2.60, 2.84]
Drug	603 (16.46)	149 (7.98)	752 (13.60)	1,648 (6.59)	325 (1.37)	1,973 (4.05)	2.96	[2.72, 3.23]	5.78	[4.79, 6.97]	3.69	[3.41, 3.99]
Violence	497 (13.56)	74 (3.96)	571 (10.32)	770 (3.08)	118 (0.50)	888 (1.82)	4.99	[4.48, 5.56]	7.90	[5.93, 10.52]	6.05	[5.46, 6.69]
Traffic	593 (16.18)	79 (4.23)	672 (12.15)	1,985 (7.94)	350 (1.48)	2,335 (4.80)	2.39	[2.20, 2.60]	2.85	[2.24, 3.62]	2.77	[2.56, 3.01]
Public-order	516 (14.08)	74 (3.96)	590 (10.67)	1,368 (5.47)	257 (1.09)	1,625 (3.35)	3.14	[2.86, 3.45]	3.62	[2.81, 4.66]	3.57	[3.26, 3.90]
Property	367 (10.02)	114 (6.11)	481 (8.70)	635 (2.54)	442 (1.87)	1,090 (2.24)	4.04	[3.56, 4.58]	3.28	[2.68, 4.00]	3.89	[3.50, 4.32]
Sexual	115 (3.14)	1 (0.05)	116 (2.10)	132 (0.53)	8 (0.03)	140 (0.29)	5.80	[4.51, 7.45]	1.60	[.20, 12.79]	7.11	[5.56, 9.09]
Other	361 (9.85)	31 (1.66)	392 (7.09)	630 (2.52)	88 (0.37)	718 (1.48)	4.26	[3.75, 4.83]	4.43	[2.95, 6.64]	5.05	[4.48, 5.70]

Note: Patients diagnosed with ADHD in 2009 to 2011 and the general population excluding those in contact with CAMHS in 2009 to 2011 aged 10 to 18 years at time of inclusion followed for 8 years, excluding those who either died (n = 95) or emigrated (n = 1,603). Age-adjusted risk ratios. ADHD = attention-deficit/hyperactivity disorder; CAMHS = Child and Adolescent Mental Health services; RR = risk ratio.

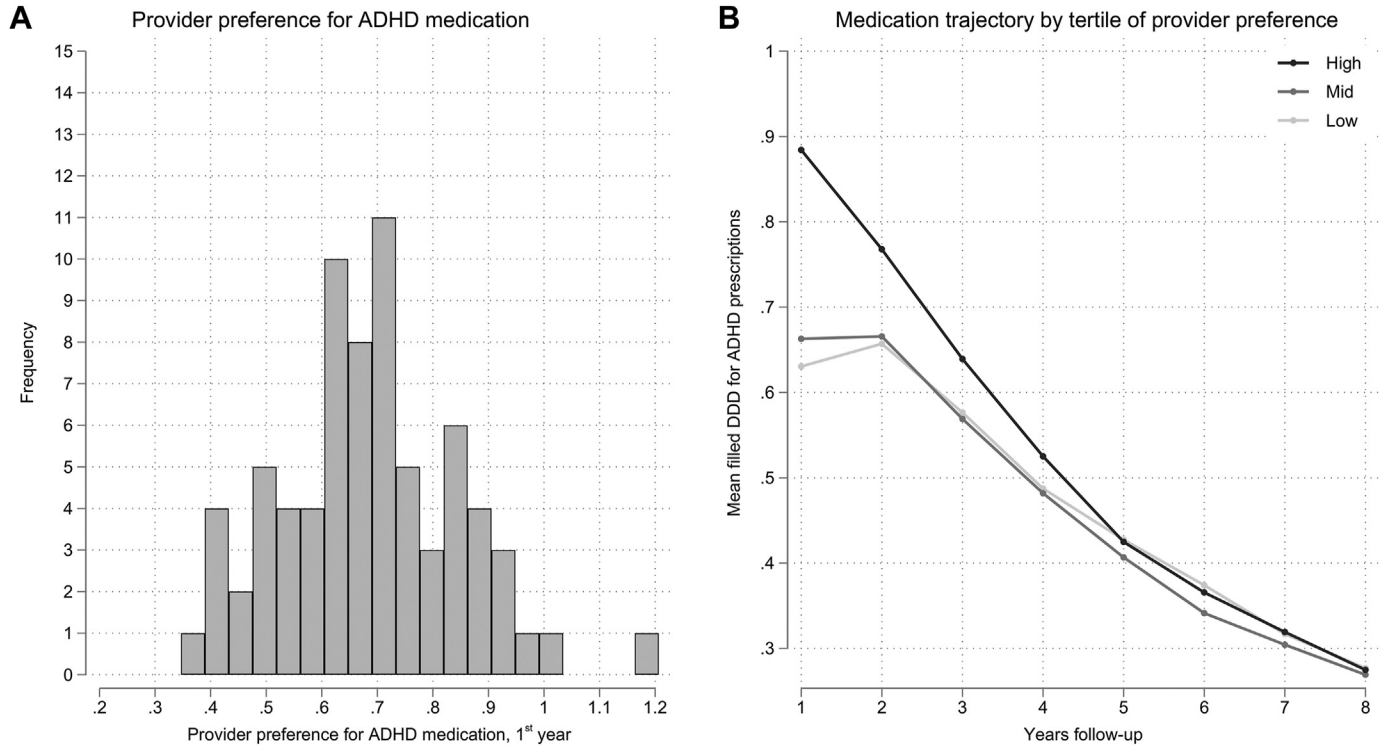
convergence across clinics in subsequent years. Nonetheless, clinics with the highest prescription practice continue prescribing more medication in later years. Instrument relevance is supported by strong first-stage F statistics for the IVs across the first years, with all values considerably above conventional thresholds for strong IVs (Figure S4A, available online).[30] There was relatively strong balance of potential instrument−outcome confounding variables, as shown by low joint F statistic values (Figure S4B, available online). There was no evidence for effects of provider preference on crime in the general population for the main IV results, which supports exclusion (Figure S5, available online).

Results for Linear Probability Models and Instrumental Variable Analyses

Figure 2 presents estimated associations between pharmacological treatment and the probability of being charged with a crime from LPMs for 1 to 4 years follow-up after ADHD diagnosis for all patients, for patients excluding F90.1, and by sex. Among all patients, patients excluding F90.1, and male patients, pharmacological treatment was negatively associated with the probability of charges for any crime, drug, violence, traffic, public order, and property. The strength of associations among all patients varied from the strongest percentage points (pp) reduction in drug-related charges (−1.9 pp, 95% CI: −2.9, −0.8) to a small positive increase in sex-related charges by 4 years (1 pp, 95% CI: 0.05, 1.5). There was no association between pharmacological treatment and criminal charges for female patients, which was a small group with few events compared to the other groups (eg, no sexual-related charges), and hence estimates are more uncertain. Estimates with large uncertainty are not reported. Probit models provided similar results (Figure S6, available online). Our main results are the IV models, with the remaining LPM results presented in Supplement 2 and Figures S7 to S10, available online.

Figure 3 presents estimated LATEs from 2SLS IV models for all patients, for patients excluding F90.1, and by sex. Pharmacological treatment reduces the probability of violence-related charges among all patients, patients excluding F90.1, and female patients over 2-year follow-up. Among all patients, pharmacological treatment reduces violence-related charges by 7.3 pp (95% CI: 13.3, 1.2). This corresponds to a number-needed-to-treat (NNT) estimate of 14, indicating that treatment intensity would have to be increased from 0 to 2 years DDDs in order for 14 patients to avoid 1 violence-related criminal charge. NNT estimates are similar for violence-related charges among patients excluding F90.1 (NNT: 13) and female patients (NNT: 10). IV results also support an effect of pharmacological treatment on public-order charges among patients excluding F90.1 at

FIGURE 1 Variation Between Clinics in Attention-Deficit/Hyperactivity Disorder (ADHD) Medication Among Patients Diagnosed With ADHD



Note: (A) Provider preference for ADHD medication at clinic level as mean defined daily doses for ADHD medication first year after ADHD diagnosis among patients on x-axis. Provider preference is scaled so that value 1 equals 365 DDD. (B) Medication trajectories. Yearly mean filled ADHD medication after diagnosis by tertiles of clinics' medication preference. DDD = daily defined doses.

3- and 4-year follow-up. Here pharmacological treatment reduces public-order charges by 12.3 pp (95% CI: 21.4, 3.1) at 3-year and 15.4 pp (95% CI: 29.7, 1.1) at 4-year follow-up. This corresponds to NNT estimates of 8 and 7, respectively. Standard errors were large. First stage was weak for female patients at year 3 and not supported in year 4; thus, these estimates are not reported.

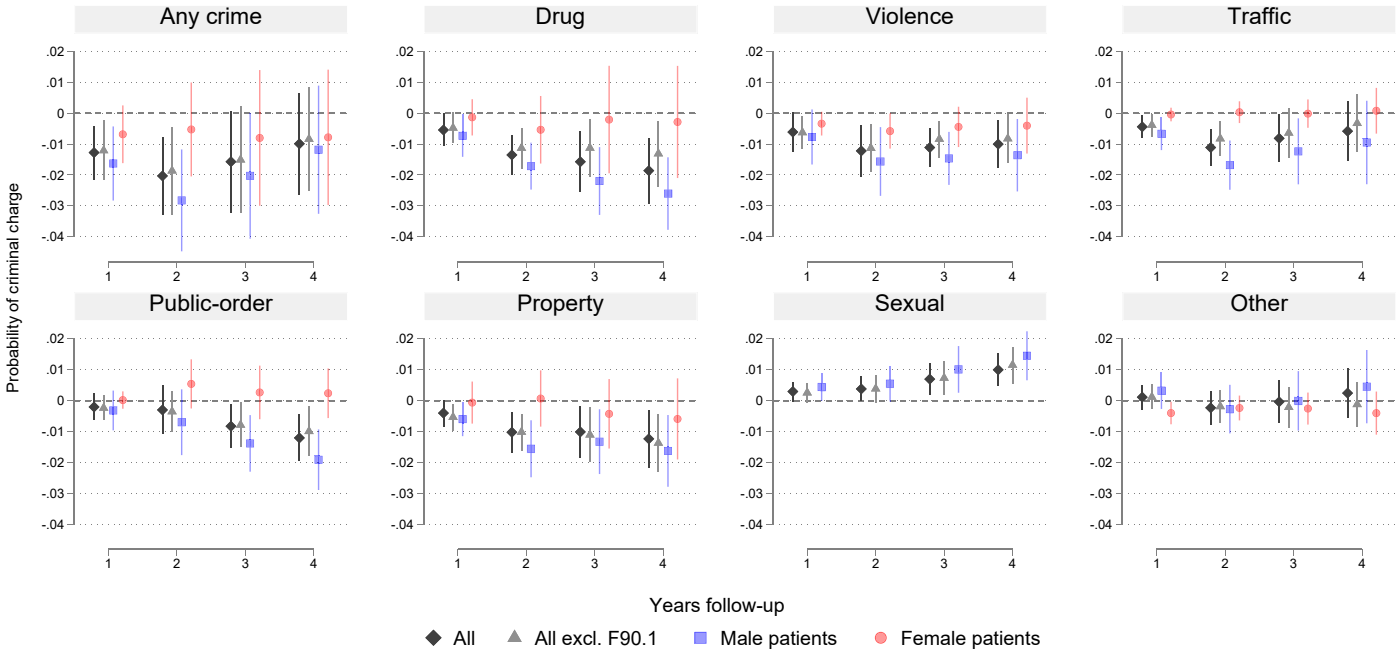
Estimated LATEs from IV Probit models gave very similar effect estimates (Figure S11, available online). These models additionally supported the following effects of pharmacological treatment: any crime for all patients at 3-year follow-up (−18.5 pp, 95% CI: −35.6, −1.3; NNT: 5); violence at first-year follow-up for all patients (−2.8 pp, 95% CI: −5.4, −0.2; NNT: 36), all patients excluding F90.1 (−3.1 pp, 95% CI: −5.5, −0.6; NNT: 33), and male patients (−4.1 pp, 95% CI: −8.0, −0.1; NNT: 25); public-order charges for all patients at 3-year follow-up (−9.2 pp, 95% CI: −16.7, −1.8; NNT: 11); traffic-related charges for all patients at 3-year follow-up (−7.1 pp, 95% CI: −13.3, −0.1; NNT: 14); property-related charges for female patients (−12.3 pp, 95% CI: −23.0, −1.7; NNT: 8) at 2-year follow-up, and all excluding F90.1 (−8.8 pp, 95% CI: −17.2, −0.3; NNT: 11) at 3-year follow-up.

IV analysis by medication type showed support for reduced violence (−6.3 pp, 95% CI: −12.3, −0.3; NNT: 16) over 2 years (Figure S12, available online), whereas estimates for non-stimulants were imprecise (Figure S13, available online). In patients 14 to 18 years of age at the time of diagnosis, there was support for reduction in violence (−20.9 pp, 95% CI: −38.0, −3.6; NNT: 5) at 2-year follow-up (Figure S14, available online). There was no support for effects in patients with only F90.1, but standard errors were large (Figure S15, available online). Most violence-related and public-order−related charges were either of low or moderate severity, corresponding to less than 1 or 1 to 3 years of prison, with more severe violence-related charges (Table S6, available online).

DISCUSSION

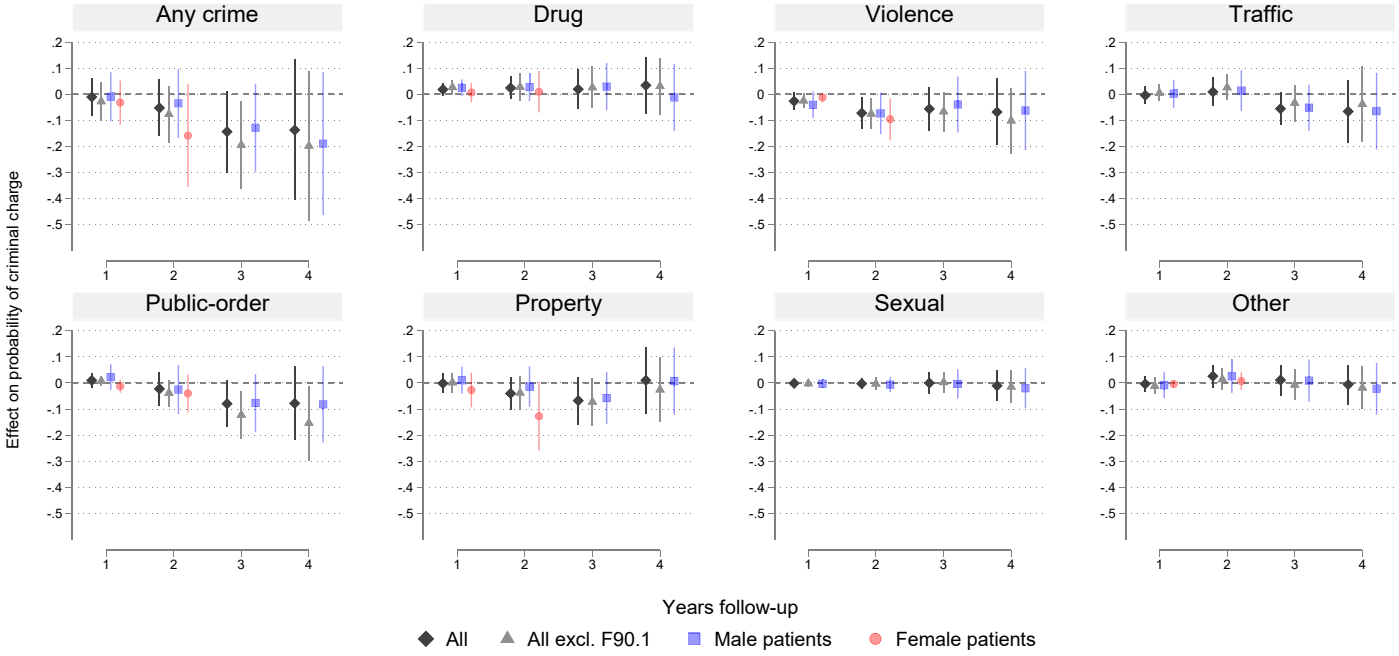
In this study, we examined the effects of pharmacological treatment of ADHD on criminality using a

FIGURE 2 Associations Between Attention-Deficit/Hyperactivity Disorder (ADHD) Medication and Criminal Charges From Linear Probability Models



Note: *Patients with ADHD diagnosis in Norway 2009 to 2011 aged 10 to 18 years at time of diagnosis. Coefficient plots for regressions with 95% CIs from LPM adjusted for patient mix. excl. = excluding; LPM = linear probability model.*

FIGURE 3 Effect Estimates of Attention-Deficit/Hyperactivity Disorder (ADHD) Medication on Criminal Charges From Instrumental Variable Analyses



Note: *Patients diagnosed with ADHD in Norway 2009 to 2011 aged 10 to 18 years at time of diagnosis. Coefficient plots for regressions with 95% CIs. Two-stage least-squares (2SLS) estimates adjusted for patient mix. excl. = excluding.*

quasi-experimental provider-preference instrumental variable design combined with nationwide registry data. Provider preference for pharmacological treatment varied considerably between clinics and strongly affected patients' treatment status. All categories of crime were elevated in children and adolescents with ADHD compared to the general population. IV analyses suggests that pharmacological treatment can have protective effects on violence-related and public-order−related crimes among patients on the margin of pharmacological treatment.

Violence and public-order crimes are often caused by impulsive−reactive behavior, which is more common in ADHD[1] and often related to social context.[31] There is no consensus on effects of pharmacological treatment of ADHD on criminality.[1,13-16] Our results are consistent with several Scandinavian studies that suggest protective effects.[2,15] A major strength of our design, relative to existing research, is that IV methods can correct for all types of unobserved confounding. Our study thus adds credible causal estimates to the evidence showing that pharmacological treatment of ADHD can reduce criminality.

Comparing estimates across studies is challenged by varying, and often not clearly stated, estimands. We presented associational estimates (using LP regressions) alongside causal estimates of the local average treatment effect (LATE).[19] Results from these 2 analyses differed, but so did their estimands and assumptions for causal inference. Our associational estimates are likely biased upward, as patients with severe ADHD symptoms select positively into both treatment and crime. IV analysis accounts for this selection bias, and the estimated treatment effects were considerably larger. IV estimates, strictly speaking, refer only to patients on the margin of treatment, not to the average patient. Moreover, IV also corrects for potential measurement error, which otherwise attenuates LP regression estimates.

The IV estimates have large standard errors, which make it difficult to detect small treatment effects and may therefore explain why the effects for which we find statistically significant evidence are substantively large. Less precision is expected, as IV uses only treatment variation induced by provider preference, whereas LPM uses all treatment variation. Treatments effects also became less precise over follow-up as the first stage weakened.

To our knowledge, only 1 other study has estimated LATE for pharmacological treatment of ADHD on crime using nationwide registry data. That study found fewer contacts with police but no reduction in charges following treatment; however, their sample size was relatively low for the latter analyses.[32]

This study has several strengths. Norway has a universal publicly funded health care system. In Norway, as in the US,[33] large geographical variation in ADHD diagnoses and medication[29,34] as well as clinicians' attitudes toward ADHD diagnoses and medication[35] suggest practice variations. Because patients are assigned to clinics based on their place of residence and cannot choose their provider due to a negligible private sector, provider preferences are plausibly random with respect to patient outcomes, especially after adjusting for patient mix, which we address with a rich set of covariates.

The use of a quasi-experimental IV design combined with rich nationwide data provides credible estimates of causal treatment effects. IV assumptions are extensively examined and supported by subject knowledge and statistical tests. Results were similar across models using LPM and 2SLS and Probit and IV Probit.[36] Treatment effects from the IV analyses are highly relevant to clinical practice. We provide evidence on whether it is beneficial to increase pharmacological treatment among patients where there likely is clinical uncertainty. Examining treatment and crime over the same time window also circumvents issues of artificial cut-offs for treatment and outcome windows.

There are also limitations to consider. First, the 2 overarching uncertainties regarding the IV design are whether variation in provider preference for medication truly is effectively random for patients (exogenous), and whether the treatment that patients receive between clinics truly differ only by medication dosage. Provider preference is arguably as good as random for patients accounting for patient mix within our institutional setting. However, we cannot entirely preclude provider-related common causes of the instrument and outcome.[37] Substantial geographical variation in ADHD symptom load has been ruled out.[34] Second, we cannot preclude clinic-wise variation in preference for psychosocial treatment. Receiving pharmacological treatment probably implies more contact with CAMHS. This introduces uncertainty as to whether the effects are due to pharmacological treatment alone. We could not adjust for psychosocial treatment, as this is not recorded in our registry data. Nonetheless, treatment effect variation by medication type showed varying effectiveness, suggesting that more contact with CAMHS is an unlikely explanation. Third, ADHD is highly heritable, causing familial aggregation,[38] and may cause interference. Detection of ADHD and treatment of 1 child may cause parents to suspect ADHD and medication benefits in siblings. We did not have access to sibling data. However, this would have to be a strong mechanism to cause concern and, to our knowledge, there is no strong evidence of this. Fourth, monotonicity in provider-preference IV designs have been

challenged, as defiers may exist because of clinicians' varying balancing of risks and benefits.[39] Analyses, however, supported a monotonic relationship between patient treatment and provider preference. Fifth, there may be measurement error related to using filled prescriptions from pharmacies for treatment and provider preference. Moreover, the general problem of underreported crimes, whether due to nondetection or non-reporting, cannot be addressed with our register data. These data are typically more reliable for some crimes (eg, drugs) than for others (eg, theft that may be prevalent in persons with ADHD). However, Norwegian register data on consumed prescriptions do not exist, and data on criminal charges are often considered to more accurately reflect societal crime relative to convictions.[40]

Reducing crime in ADHD populations is an important priority for society and in the interest of the individual patients and their immediate family. The observed variation in rates of pharmacological treatment of ADHD is likely caused partly by variation in provider preferences, that is, variation in clinicians' attitudes toward medication in patients with ADHD,[34,35] and the clinical implication of this study may be affected by clinicians' positions on the ADHD controversy. Clinicians with a liberal attitude toward ADHD medication are typically concerned about adverse long-term outcomes in untreated ADHD, including, for example, elevated risk of criminality. These clinicians are optimistic that pharmacological treatment may reduce such adverse outcomes. These findings may be taken as empirical support of the liberal position on pharmacological treatment in ADHD. On the contrary, clinicians with a restrictive position regarding pharmacological treatment are concerned about over-treatment, medicalization, and unnecessary side effects. They may question whether pharmacological treatment in an additional 8 to 14 children with ADHD is justified to prevent a public-order–related or violence-related criminal charge among 1 of these children. Most public-order–related and violence-related charges were of low to moderate severity (Table S6, available online), which is of relevance in treatment decisions. The lack of support for protective effects of medication in the remaining categories of crime may be read as supporting the restrictive position. Nonetheless, clinical decision making for pharmacological treatment of ADHD relies on many considerations, of which crime reduction is one.

In conclusion, this is the first study to demonstrate causal effects of pharmacological treatment of ADHD on some types of crimes in a population-based natural experiment. Pharmacological treatment of ADHD reduced crime related to impulsive–reactive behavior in patients with ADHD on the margin of treatment, whereas no effects were found on crimes requiring criminal intent, conspiracy, and planning.

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Author Contributions

TW: Conceptualization, methodology, data curation, formal analysis, visualization, funding acquisition, project administration, writing-original draft, writing-review & editing. HZ: Conceptualization, supervision, methodology, writing-review & editing. SM: Conceptualization, supervision, methodology, writing-review & editing. FE: Conceptualization, methodology, writing-review & editing. IL: writing-review & editing. AC: writing-review & editing. IB: Conceptualization, supervision, writing-review & editing. AH: Conceptualization, supervision, writing-review & editing. KR: Conceptualization, writing-review & editing. AM: Conceptualization, funding acquisition, methodology, supervision, project administration, writing-review & editing.

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