ORIGINAL ARTICLE

Medication for Attention Deficit–Hyperactivity Disorder and Criminality

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ABSTRACT

BACKGROUND

Attention deficit–hyperactivity disorder (ADHD) is a common disorder that has been associated with criminal behavior in some studies. Pharmacologic treatment is available for ADHD and may reduce the risk of criminality.

METHODS

Using Swedish national registers, we gathered information on 25,656 patients with a diagnosis of ADHD, their pharmacologic treatment, and subsequent criminal convictions in Sweden from 2006 through 2009. We used stratified Cox regression analyses to compare the rate of criminality while the patients were receiving ADHD medication, as compared with the rate for the same patients while not receiving medication.

RESULTS

As compared with nonmedication periods, among patients receiving ADHD medication, there was a significant reduction of 32% in the criminality rate for men (adjusted hazard ratio, 0.68; 95% confidence interval [CI], 0.63 to 0.73) and 41% for women (hazard ratio, 0.59; 95% CI, 0.50 to 0.70). The rate reduction remained between 17% and 46% in sensitivity analyses among men, with factors that included different types of drugs (e.g., stimulant vs. nonstimulant) and outcomes (e.g., type of crime).

CONCLUSIONS

Among patients with ADHD, rates of criminality were lower during periods when they were receiving ADHD medication. These findings raise the possibility that the use of medication reduces the risk of criminality among patients with ADHD. (Funded by the Swedish Research Council and others.)

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About 5% of all children in the Western world fulfill diagnostic criteria for attention deficit–hyperactivity disorder (ADHD),[1] and a large proportion of such children are treated pharmacologically.[2] ADHD has been associated with criminality[3,4] and externalizing disorders.[5] Beneficial short-term effects of ADHD medication on symptoms of ADHD and associated conduct problems have been shown in numerous randomized, controlled studies involving children[6-8] and adults.[9-11] ADHD symptoms are largely persistent from childhood into adulthood,[12] but one prominent feature of ADHD treatment is that the discontinuation of medication is common,[13,14] especially in adolescence and early adulthood.[15] The importance of treatment discontinuation for criminality and other longer-term outcomes is largely unknown.

The Multimodal Treatment of Attention Deficit–Hyperactivity Disorder (MTA) study is the largest randomized clinical trial of ADHD medication with long-term follow-up.[16-19] The most sensitive measures of treatment (a composite of ADHD symptoms, as rated by parents and teachers) suggested that the benefit of medication at the 14-month assessment had diminished at 36 months.[20] No association was observed with early delinquency and substance use at 36 months.[19] Although the study did not suggest long-term effects of medication, high rates of treatment discontinuation, a lack of placebo-treated controls, and a limited range of outcomes mean that the longer-term effects of ADHD medication remain uncertain. In this study, we used Swedish population-based data to investigate the association between the use of ADHD medication and criminality.

Methods

Patients

The study was approved by the ethics committee at Karolinska Institutet. We derived the data through linkage of population-based registers in Sweden, with unique personal identification numbers, enabling accurate linkage.[21] We identified 25,656 patients (16,087 men and 9569 women) who had been born no later than 1990 with at least one diagnosis of ADHD (as defined by code 314 in the *International Classification of Diseases, 9th Revision* [ICD-9]; and code F90 in ICD-10) in the National Patient Register. These patients included all those with psychiatric hospitalizations since 1973 and outpatient diagnoses since 2001.[22] We also used the Prescribed Drug Register, which includes information on all prescribed medications since July 2005.[23] A general population sample was used to contrast rates of criminality and medication use between patients with an ADHD diagnosis and the general population. To ensure adequate statistical power and equal follow-up time, we matched 10 controls to each case according to the year of birth, sex, and geographic location at the time of diagnosis.

Criminality was identified through the National Crime Register, including convictions in district courts since 1973,[24] and the Register of Persons Suspected of Offenses, which records all persons suspected of a crime after a completed investigation by police, customs authority, or the prosecution service.[24]

To account for migrations, deaths, and imprisonment, we linked to the Migration, Cause of Death, and Prison Registers. We estimated periods that patients had spent in closed institutional youth care using conviction data in the National Crime Register.

Measures

We measured the main exposure of patients to ADHD medication, as identified in the Prescribed Drug Register, using the Anatomical Therapeutic Chemical (ATC) classification system. Before 2008, ADHD medication could be prescribed only by child and adolescent psychiatrists, neuropediatricians, or physicians who had been licensed after individual application and Medical Products Agency approval. Since then, all specialists in psychiatry are licensed to prescribe such drugs.

Since 2005, the use of ADHD medication in both children and adults has increased exponentially.[14] Methylphenidate is recommended for first-line drug treatment, whereas amphetamine and dextroamphetamine are prescribed more rarely. The nonstimulant atomoxetine is also used regularly.[14]

In accordance with previous studies,[14,15] a patient was defined as receiving treatment during the time interval between two prescriptions of ADHD medication, unless prescriptions occurred more than 6 months apart. Thus, a treatment period was defined as a sequence of prescriptions, with no more than 6 months between two consecutive prescriptions. The start of treatment was defined

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Table 1. Characteristics of the Patients at Baseline and Rates of Use of ADHD Medication and Criminal Convictions during Follow-up.*

Characteristic	Men (N=16,087)	Women (N=9569)
Person-years at risk	62,637	37,963
Age group (%)		
15–24 yr	54.3	46.3
25–39 yr	30.0	35.4
≥40 yr	15.7	18.3
Civil status (%)		
Unmarried	85.7	73.4
Married	7.5	13.1
Divorced	6.7	13.2
Widowed	0.1	0.4
Living in a metropolitan area (%)	14.8	15.1
Employed (%)	24.3	25.6
In school (%)	29.2	29.5
Median family income (in U.S. $)	27,500	26,500
Taking other psychotropic medication (%)		
Antipsychotic drug	11.9	13.1
Hypnotic or anxiolytic drug	27.3	39.1
Antidepressant drug	28.7	45.1
Drug used in addictive disorders	4.6	3.1
Mood stabilizer or antiepileptic agent	8.2	11.1
Receiving ADHD medication (%)	53.6	62.7
Convicted of any crime (%)	36.6	15.4
Less severe crime†	34.4	15.0
Violent or sexual crime	14.7	3.6
Homicide	0.13	0.04
Assault	9.3	2.0
Threat or harassment	6.3	1.1
Threat or assault against a public servant	3.2	1.1
Robbery	1.6	0.0
Arson	0.2	0.1
Sexual crime	0.7	0.0
Substance-related crime	20.5	7.9
Drug offense	17.7	7.2
Driving under the influence of drugs	9.4	2.5

* Data are for patients in the Swedish Patient Register with a diagnosis of ADHD who were born in 1990 or earlier.

† A less severe crime was defined as one in which a conviction did not involve imprisonment, forensic psychiatric inpatient care, or closed institutional youth care.

as the date of the first prescription, and the end of treatment was defined as the date of the last prescription. During intervals of 6 months or more without any prescriptions, a patient was considered not to be receiving treatment. A total of 914 patients who received only one prescription were considered not to have received treatment. To determine whether patients were receiving treatment at the start and end of follow-up, the follow-up period was defined as January 1, 2006, to December 31, 2009, since the Prescribed Drug Register covered the period only from July 1, 2005, to June 30, 2010.

The main outcome was any conviction for a crime. If no date of the crime was recorded, the date of the conviction was used. In sensitivity analyses, we also investigated less severe crimes (i.e., those not associated with custodial sentences) along with violent crime and those related to substance abuse.[25] (Crime categories and prevalence are provided in Table 1.)

We identified patients with diagnoses of conduct disorders, as well as oppositional–defiant, antisocial-personality, or substance-use disorder, through the National Patient Register (codes 313.81, 312, 301.7, 291, 292, 303, 304, and 305 in the ICD-9; and F91, F60.2, and F10–F19 in the ICD-10).

STATISTICAL ANALYSIS

In all analyses, the use of an ADHD medication was treated as a time-varying covariate. To describe unadjusted associations between the use of ADHD medication and criminality, we calculated extended Kaplan–Meier curves for time-varying covariates.[26] This analysis can be viewed as a nonparametric analogue to Cox regression with time-varying covariates. If the association between current medication use and conviction rates was independent of previous medication use, then the extended Kaplan–Meier curves could be interpreted as estimated survival functions for patients who did not change their medication status during follow-up.[27] To quantify the adjusted association between medication use and criminality, we used Cox regression hazard ratios, with robust standard errors accounting for the correlations between periods for the same patient.[28]

Next, we used stratified Cox regression to perform within-patient analyses, with adjustment for age, previous number of convictions, and previous number of medication switches as categorical variables in the model. In stratified Cox regression, each patient enters as a separate stratum in the analyses. Thus, each patient serves as his or her own control, and provided that the regression

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model is correct, these analyses adjust for confounders that are constant within each patient during follow-up (e.g., genetic makeup and childhood environment). A thorough description of the statistical analysis plan is provided in the Supplementary Appendix, available with the full text of this article at NEJM.org.

It is possible that an association between medication use and criminality may be seen when patients who have decided to start taking a medication have also decided to make other significant changes in their lives. We addressed this potential confounder by investigating whether associations with criminality were different when patients went from a treatment period to a nontreatment period, as compared with when they went from a nontreatment period to a treatment period. We evaluated patients with consecutive periods in which they had different medication statuses and estimated the difference in risk for criminality for nontreatment periods versus treatment periods. Confidence intervals were estimated by means of the nonparametric bootstrap methods. We also examined whether these associations were consistent according to whether a patient was prescribed an ADHD medication for the first or second time.

In order to understand whether observed associations could be explained by selection and to test the robustness of our results, we performed nine post hoc analyses, including evaluations of different drug exposures (stimulant vs. nonstimulant treatment) and outcomes (convictions for less severe, violent, or substance-related offenses).

We performed sensitivity analyses in a cohort of patients who did not necessarily have an ADHD diagnosis in the National Patient Register. Instead, the Prescribed Drug Register was used to identify patients who had received at least one prescription for an ADHD medication during follow-up. This was done to avoid selection bias, since some counties have historically been less consistent in reporting outpatient data to the National Patient Register.

The patients in our main analyses had received a diagnosis of ADHD, as reported to the National Patient Register by a specialist physician. Sensitivity analyses were therefore performed in a cohort who had received the diagnosis by practitioners (physicians, psychologists, or other nonmedical specialists) in general child and adolescent mental health services. For this, we linked to the Pastill Register, which includes patients who had received diagnoses according to the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) or the ICD-10 since 2001 within Child and Adolescent Mental Health Services in Stockholm County.[29]

Since the diagnosis of ADHD often coexists with conduct, oppositional–defiant, antisocial-personality, or substance-use disorder,[5] it is not clear whether these disorders should be regarded as confounders, mediators, or colliders.[30] Thus, to test whether the association between medication use and criminality was different depending on coexisting diagnoses, we performed a sensitivity analysis that included only patients without a diagnosis of a coexisting disorder.

In Sweden, persons who are found guilty of crimes are convicted regardless of mental disorder, although sentencing will be influenced by psychiatric evidence. Nevertheless, the probability of receiving a conviction might be dependent on socioeconomic conditions, living area, or the age or psychiatric history of the person. Therefore, we also performed sensitivity analyses that included persons who had been suspected of (rather than sentenced for) crimes.

To test whether associations were restricted to ADHD medication, we also performed sensitivity analyses that included patients who discontinued taking a selective serotonin-reuptake inhibitor (SSRI) instead of an ADHD medication.

To investigate long-term associations, we performed a Cox regression analysis for the period from January 2009 through December 2009, with medication status at January 1, 2006, as the main exposure. The analysis was adjusted for age and medication use during 2009 as time-dependent covariates.

RESULTS

USE OF ADHD MEDICATION AND CRIMINALITY

We investigated 16,087 men and 9569 women with ADHD (see Table 1 for descriptive data at baseline and during follow-up). Among the men in whom ADHD was diagnosed, 53.6% had taken an ADHD medication, and 36.6% had been convicted of at least one crime during follow-up. The corresponding numbers in the matched general-population controls were 0.2% and 8.9%, respectively. Among female patients, 62.7% had taken an ADHD medication, and 15.4% had been con-

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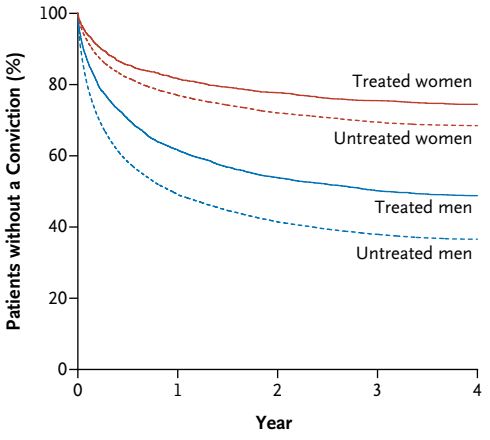

Figure 1. Extended Kaplan–Meier Curves for Patients in the Swedish Patient Register with a Diagnosis of ADHD Who Were Born No Later Than 1990, According to Sex and Medication Status.

This analysis was based on 56,227 treatment or nontreatment periods and 23,693 convictions involving 16,087 men (averaging 3.5 periods of treatment or nontreatment and 1.5 convictions) and 23,533 treatment or nontreatment periods and 4112 convictions involving 9569 women (averaging 2.5 treatment or nontreatment periods and 0.4 convictions).

victed of at least one crime, as compared with 0.1% and 2.2% among controls. A total of 689 men (4.3%) and 368 women (3.8%) were receiving ADHD medication during the entire period, and 7468 men (46.4%) and 3573 women (37.3%) were not receiving ADHD medication.

In patients with ADHD, crimes occurred less often during periods in which they were receiving an ADHD medication (Fig. 1). The estimated probability of not being convicted of a crime during a 4-year treatment period was 0.49 for men and 0.75 for women. The same probability during the nontreatment period was 0.37 for men and 0.69 for women. The unadjusted Cox regression hazard ratio was 0.70 (95% confidence interval [CI], 0.66 to 0.75) for men and 0.78 (95% CI, 0.68 to 0.90) for women, indicating that medication use was associated with a lower criminality rate (Table 2).

Since patients receiving medication might be different from untreated patients, a critical test of the association was whether there were differences in crime rates in the same person during treatment periods, as compared with nontreatment periods. The stratified Cox regression estimates of the within-patient hazard ratios were 0.68 for men and 0.59 for women ($P<0.001$ for both comparisons), suggesting that after adjustment for all confounders that are constant within a patient, the use of ADHD medication reduced the criminality rate by 32 to 41% (Table 2).

Table 2. Hazard Ratio for Conviction for Any Crime during a Period of Treatment with an ADHD Medication, as Compared with a Nontreatment Period (2006–2009).*

Sex	No. of Patients	No. of Crimes	Hazard Ratio (95% CI)	
			Cox Regression	Stratified Cox Regression
Men	16,087	23,693	0.70 (0.66–0.75)	0.68 (0.63–0.73)
Women	9,569	4,112	0.78 (0.68–0.90)	0.59 (0.50–0.70)

* Data are shown as the within-patient hazard ratio for the risk of conviction for a crime while receiving an ADHD medication, as compared with the risk while not receiving a medication. Hazard ratios were calculated with the use of Cox regression (comparing periods in which all patients received treatment with periods in which they did not receive treatment) or stratified Cox regression (comparing periods in which patients who changed their treatment status during follow-up received treatment with periods in which they did not receive treatment).

SENSITIVITY ANALYSES

Because of the clear association between medication use and criminality rate, we performed a series of sensitivity analyses that included men only, because of the increased prevalence of ADHD and criminality, as compared with women. In patients who had both treatment periods and nontreatment periods, the risk of being convicted of a crime was significantly increased, by 12.0% (95% CI, 11.8 to 12.3), during a nontreatment period, as compared with a treatment period (Table 3). The increased risk remained when patients moved from a nontreatment period to a treatment period (an increase of 15.8%) as well as when they moved from a treatment period to a nontreatment period (an increase of 6.5%). The risk remained significant regardless of whether it was the first or second time that patients altered their medication regimen (Table 3).

We found similar reductions in criminality rates associated with the use of ADHD medication regardless of whether the drug was a stimulant (hazard ratio, 0.66) or a nonstimulant (hazard ratio, 0.76) or whether analyses were restricted to less severe or specific crimes (Table 4). The hazard ratios did not materially change when patients were identified solely on the basis of their

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Table 3. Differences in the Risk of a Criminal Conviction, According to Change in Treatment with ADHD Medication.*

Treatment Period	Two Consecutive Periods		From No Medication to Medication		From Medication to No Medication	
	No. of Patients	Risk Difference (95% CI)	No. of Patients	Risk Difference (95% CI)	No. of Patients	Risk Difference (95% CI)
		%		%		%
All treatment periods	7895	12.0 (11.8–12.3)	7189	15.8 (15.4–16.1)	4736	6.5 (6.2–6.9)
First treatment period only	7398	10.4 (10.1–10.7)	6105	13.7 (13.3–14.1)	4413	5.7 (5.3–6.2)
Second treatment period only	1807	9.8 (9.3–10.4)	1788	12.0 (11.3–12.7)	1030	6.3 (5.5–7.1)

* Patients were evaluated between two consecutive periods (i.e., a period in which they did not receive treatment with an ADHD medication, as compared with a period in which they did receive treatment with an ADHD medication) and when they changed their medication status (going from nontreatment to treatment or vice versa).

prescriptions (hazard ratio, 0.64), from general child and adolescent mental health services on the basis of the Pastill Register (hazard ratio, 0.83), and when patients with a diagnosis of a coexisting disorder (conduct, oppositional–defiant, antisocial-personality, or substance-use disorder) were excluded (hazard ratio, 0.77), although the estimate did not reach significance on the basis of data from the Pastill Register (Table 4). When the outcome was changed to suspicion of a crime, there was also a reduction in the criminality rate during the treatment period (hazard ratio, 0.81). In contrast to the results for the use of ADHD medication, there was no evidence of an association between a criminal conviction and the use of an SSRI among patients with a diagnosis of ADHD in the National Patient Register) (hazard ratio, 1.04; 95% CI, 0.93 to 1.17).

LONG-TERM ASSOCIATIONS

Finally, we addressed long-term associations by exploring the medication status on January 1, 2006, and criminality rates during 2009. There was no significant association before adjustment for medication use in 2009 (hazard ratio, 0.84; 95% CI, 0.69 to 1.03) or after such adjustment (hazard ratio, 0.94; 95% CI, 0.83 to 1.07).

DISCUSSION

There has been considerable debate over the net effects of pharmacologic treatment of patients with ADHD, in which benefits with respect to ADHD symptoms are weighed against the risks of side effects,[31,32] potential overprescription, and development of tolerance, dependence, or addiction.[32,33] We found associations suggesting the possibility of a protective effect for the use of ADHD medications on concurrent rates of all types of criminality and no significant long-term reduction in the crime rate after termination of medication — findings that corroborate the results of previous randomized, short-term follow-up studies of ADHD symptoms and associated conduct problems.[6-11] Among men, the crime rate was reduced by 32% (P<0.001) during treatment periods, and the rate reduction ranged from 17 to 46% in all nine sensitivity analyses (in which the comparison was significant in eight). We observed a similar association among women, with a reduction in the crime rate of 41% (P<0.001) during treatment periods.

To avoid possible bias from reverse causation (i.e., that patients stop treatment because of their criminal behavior, rather than the other way around), we investigated whether the order of the change in medication status was important. The associations were significant regardless of the order.

Our main analyses did not address the question of whether there are only concomitant associations or whether criminality rates were affected beyond treatment termination. It is possible that pharmacologic ADHD treatment helps patients to better organize their lives or contributes to enduring changes at the neuronal level.[34] Another possibility is that the concomitant associations with treatment do not persist, which could be an explanation for previous findings of a lack of long-term effects.[17] In line with the latter possibility, we found no significantly persistent association between medication use in 2006 and the crime rate in 2009, an interpretation also supported by our finding of an as-

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Table 4. Sensitivity Analyses among Men with ADHD, According to Types of Cohort, Medication, and Criminal Outcome (2006–2009).*

Types of Cohort, Medication, and Criminal Outcome	No. of Patients in Cohort	No. of Crimes	Hazard Ratio (95% CI)
ADHD diagnosed in National Patient Register	16,087		
Stimulant drug and any criminal conviction†		23,693	0.66 (0.61–0.71)
Nonstimulant drug and any criminal conviction†		23,693	0.76 (0.63–0.91)
ADHD medication			
Violent crime		3,985	0.54 (0.44–0.67)
Less severe crime‡		17,421	0.67 (0.62–0.73)
Drug-related crime		8,502	0.63 (0.55–0.71)
No coexisting disorder and any criminal conviction§		5,723	0.77 (0.66–0.90)
Suspected of crime		55,953	0.81 (0.77–0.84)
SSRI medication and any criminal conviction		23,693	1.04 (0.93–1.17)
Prescribed ADHD medication and any criminal conviction¶	17,141	27,416	0.64 (0.60–0.68)
Pastill Register, use of ADHD medication, and any criminal conviction‖	1,090	995	0.83 (0.54–1.29)

* SSRI denotes selective serotonin-reuptake inhibitor.
† Values in this category have not been adjusted for the concomitant use of other ADHD medications.
‡ A less severe crime was defined as one in which a conviction did not involve imprisonment, forensic psychiatric inpatient care, or closed institutional youth care.
§ This category includes only patients who had not received a diagnosis of a conduct, oppositional–defiant, antisocial-personality, or substance-use disorder. This analysis was performed in a subgroup of 9801 patients.
¶ In this category, the ADHD medication was identified through the Prescribed Drug Register on the basis of Anatomical Therapeutic Chemical (ATC) codes N06BA04, N06BA09, N06BA01, and N06BA02.
‖ Patients who are listed in the Pastill Register include all those in whom ADHD was diagnosed by practitioners in child and adolescent mental health services.

sociation between medication use and criminality regardless of whether it was the first or second time that patients changed their medication status.

Unlike randomized, controlled trials, pharmacoepidemiologic studies such as this one are open to confounding because of differences in the indications for the drug. In other words, patients who are receiving treatment are different from those who are not receiving treatment, usually because they are more symptomatic and have coexisting disorders.[35] Our within-patient analyses were designed to account for confounders that remain constant for each patient (e.g., genetic and early environmental factors). However, unmeasured confounders and mediators that are related to the use of prescription drugs (e.g., alcohol binges, engagement with services that provide prescriptions, or supportive partners or parents who collect the prescriptions) rather than the effects of the drugs themselves can never be excluded in this research design. To address this problem, we analyzed criminality rates among patients who had discontinued SSRIs instead of ADHD medications. We found no evidence of an association between criminality rates and SSRI discontinuation. In contrast to ADHD medications, other common psychotropic drugs have very different patterns of use as well as onset and end of effect. Thus, such drugs could not be included as time-dependent covariates in our study, but at the same time, it is unlikely that the use of psychotropic (or other) medications would have the potential to explain the concomitant association between the use of ADHD medication and criminality. Selection effects might also occur, since the registration of outpatient diagnoses started in 2001 and is still not complete in all counties; in addition, only treatments by specialist physicians are entered into the National Patient Register, and some patients (e.g., those with more severe ADHD or living in neighborhoods with a lower socioeconomic status) might be more likely to be convicted when caught. We tried to address selection biases by doing sensitivity analyses among

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different cohorts and with varying outcomes. All analyses suggested that there were reductions of 17 to 46% in criminality rates during treatment periods, findings that reduced the likelihood that our results were due to selection effects.

Overall rates of crime and their resolution are very similar across Western Europe,[36] whereas comparisons with the United States are more difficult because of differences in the legal and judicial systems. Police-recorded assault rates were 3.7 per 1000 population in the United States and 4.1 per 1000 in Sweden from 1981 through 1999.[37] Even though the prevalence of ADHD diagnoses and rates of medication use vary among countries and over time, Sweden does not appear to be unusual in its rates of ADHD or the use of ADHD medication.[38,39] The Swedish Medical Products Agency recommends pharmacologic treatment for ADHD only when other supportive interventions have failed, indicating that pharmacologic ADHD treatment most likely represents an indicator of the more severe cases of ADHD. Regardless, we cannot address whether the associations would be the same in other cultures, and thus generalizations should be made with caution.

Among patients with ADHD, we found an inverse association between pharmacologic treatment for ADHD and the risk of criminality. Potential beneficial effects would have to be carefully weighed against potential adverse effects of medication, including overprescription and side effects.[31,33]

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