

Association Between Prescription of Major Psychotropic Medications and Violent Reoffending After Prison Release

Zheng Chang, PhD; Paul Lichtenstein, PhD; Niklas Långström, MD; Henrik Larsson, PhD; Seena Fazel, MD

IMPORTANCE Individuals released from prison have high rates of violent reoffending, and there is uncertainty about whether pharmacological treatments reduce reoffending risk.

OBJECTIVE To investigate the associations between major classes of psychotropic medications and violent reoffending.

DESIGN, SETTING, AND PARTICIPANTS This cohort study included all released prisoners in Sweden from July 1, 2005, to December 31, 2010, through linkage of population-based registers. Rates of violent reoffending during medicated periods were compared with rates during nonmedicated periods using within-individual analyses. Follow-up ended December 31, 2013.

EXPOSURES Periods with or without dispensed prescription of psychotropic medications (antipsychotics, antidepressants, psychostimulants, drugs used in addictive disorders, and antiepileptic drugs) after prison release. Prison-based psychological treatments were investigated as a secondary exposure.

MAIN OUTCOMES AND MEASURES Violent crime after release from prison.

RESULTS The cohort included 22 275 released prisoners (mean [SD] age, 38 [13] years; 91.9% male). During follow-up (median, 4.6 years; interquartile range, 3.0-6.4 years), 4031 individuals (18.1%) had 5653 violent reoffenses. The within-individual hazard ratio (HR) associated with dispensed antipsychotics was 0.58 (95% CI, 0.39-0.88), based on 100 events in 1596 person-years during medicated periods and 1044 events in 11 026 person-years during nonmedicated periods, equating to a risk difference of 39.7 (95% CI, 11.3-57.7) fewer violent reoffenses per 1000 person-years. The within-individual HR associated with dispensed psychostimulants was 0.62 (95% CI, 0.40-0.98), based on 94 events in 1648 person-years during medicated periods and 513 events in 4553 person-years during nonmedicated periods, equating to a risk difference of 42.8 (95% CI, 2.2-67.6) fewer violent reoffenses per 1000 person-years. The within-individual HR associated with dispensed drugs for addictive disorders was 0.48 (95% CI, 0.23-0.97), based on 46 events in 1168 person-years during medicated periods and 1103 events in 15 725 person-years during nonmedicated periods, equating to a risk difference of 36.4 (95% CI, 2.1-54.0) fewer violent reoffenses per 1000 person-years. In contrast, antidepressants and antiepileptics were not significantly associated with violent reoffending rates (HR = 1.09 [95% CI, 0.83-1.43] and 1.14 [95% CI, 0.79-1.65], respectively). The most common prison-based program was psychological treatments for substance abuse, associated with an HR of 0.75 (95% CI, 0.63-0.89), which equated to a risk difference of 23.2 (95% CI, 10.3-34.1) fewer violent reoffenses per 1000 person-years.

CONCLUSIONS AND RELEVANCE Among released prisoners in Sweden, rates of violent reoffending were lower during periods when individuals were dispensed antipsychotics, psychostimulants, and drugs for addictive disorders, compared with periods in which they were not dispensed these medications. Further research is needed to understand the causal nature of this association.

JAMA. 2016;316(17):1798-1807. doi:10.1001/jama.2016.15380

← Editorial page 1771

+ Supplemental content

+ CME Quiz at
jamanetworkcme.com

Author Affiliations: Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden (Chang, Lichtenstein, Långström, Larsson); Department of Psychiatry, Warneford Hospital, University of Oxford, Oxford, England (Chang, Fazel); Department of Neuroscience, Uppsala University, Uppsala, Sweden (Långström); School of Medical Sciences, Örebro University, Örebro, Sweden (Larsson).

Corresponding Author: Seena Fazel, MD, Department of Psychiatry, Warneford Hospital, University of Oxford, Oxford OX3 7JX, England (seena.fazel@psych.ox.ac.uk).

There were more than 10 million prisoners worldwide in 2015, with approximately 2.2 million in the United States alone.¹ Despite reported decreases in violence in many countries, reoffending rates remain high. From 2005 through 2010, more than one-third of released prisoners in the United States and the United Kingdom were reconvicted of a new crime within 2 years.^{2,3} With planned reductions in prison populations in many countries, evidence to facilitate the safe release of large numbers of prisoners has become a research and policy priority.⁴

Most programs to reduce reoffending focus on psychosocial interventions, but their effect sizes are weak to moderate.⁵ As psychiatric and substance use disorders, which increase reoffending rates,⁶ are overrepresented among jail and prison populations,⁷ treatment with appropriate psychotropic medications offers an alternative strategy to reduce reoffending. In the general population, randomized clinical trials⁸ and observational studies^{9,10} have demonstrated associations between psychotropic medications and reductions in violence and crime. However, the evidence to modify reoffending risk is limited to a few small observational studies.¹¹⁻¹³ Two major methodological issues restrict their validity. First, pharmacoepidemiologic studies are subject to confounding because of differences in indications for medication.¹⁴ That is, prisoners who are prescribed psychotropic medications are different (eg, more severe symptoms, comorbidity, or background risk) from those who are not. Second, nonadherence with medications is common in psychiatric patients,¹⁵ so more sensitive measures of medication exposure than simple categorization into treatment and nontreatment groups are required, as are approaches that account for individual differences in medication adherence.

This study investigated the main psychotropic medication classes prescribed to prisoners using longitudinal Swedish population registers and examined the association between prescription of psychotropic medication and risk of violent reoffending. For comparison, the associations of prison-based psychological treatments with reoffending were secondarily investigated.

Methods

Study Population

Data were obtained through linkage of population-based registers in Sweden, with unique personal identification numbers enabling accurate linkage.¹⁶ The study cohort consisted of all prisoners released between July 1, 2005, and December 31, 2010, from the Swedish Prison and Probation Service (SPPS). In addition to implementing sentences, the SPPS aims to reduce criminal recidivism and substance misuse by providing group-based, usually cognitive behavioral therapy-based programs. Complementary education and work skills training are also offered. In any given day, SPPS staff manage some 5000 inmates in 50 prisons and an additional 12 500 parolees or probationers across 34 probation offices all over Sweden.¹⁷

All individuals were followed up from the day of release until death, emigration, reincarceration, or December 31, 2013,

Key Points

Question Is the use of psychotropic medications associated with a lower risk of reoffending for violent crime among released prisoners?

Findings In this cohort study of 22 275 released prisoners, 3 classes of psychotropic medications (antipsychotics, psychostimulants, and medications used for addictive disorders) were associated with statistically significant hazard ratios (0.58, 0.62, and 0.48, respectively) of violent reoffending.

Meaning Evidence-based provision of psychotropic medications to released prisoners was associated with lower risk of reoffending.

whichever happened first. The study was approved by the Regional Ethics Committee at Karolinska Institutet, Stockholm, Sweden, which waived the requirement of informed consent because this study is a register-based study of anonymized data.

Measures

Data on the main exposure, psychotropic medications, were extracted from the Prescribed Drug Register, which includes information on all dispensed medication in Sweden since July 2005.¹⁸ The register also collects dispensing data for individuals in all forms of detention, including prisons. Following the Anatomical Therapeutic Chemical (ATC) classification system, 4 classes of psychotropic medications commonly used in this sample were selected: antipsychotics were defined with ATC code N05A; antidepressants with ATC code N06A; psychostimulants with ATC code N06B; and drugs used in addictive disorders with ATC code N07B, including nicotine, varenicline, disulfiram, acamprosate, naltrexone, buprenorphine, and methadone. Antiepileptic drugs (ATC code N03A), a mixed medication class used for treatment of epileptic seizures, neuropathic pain, and mood instability, were also included. Adrenergic inhalants (ATC code R03A), a commonly used medication class with negligible psychotropic effects, were selected as a negative control.

For each medication class, medication status was treated as a time-varying exposure (ie, medication status was not necessarily constant through follow-up), and each individual's follow-up was divided into medicated and nonmedicated periods. In accordance with previous studies,^{9,10} an individual was defined as exposed to medication during the interval between 2 dispensed prescriptions, unless prescriptions were issued more than 3 months apart. We chose this interval because in routine psychiatric practice, oral medications are unlikely to be dispensed for more than 3 months at a time (the so-called 90-day rule in Sweden).⁹ The start of medication was defined as the date of the first prescription, and the end of medication was defined as the date of the last prescription. During intervals of 3 months or longer without any prescriptions, an individual was considered not exposed to medication. Each of the medication classes was considered independently, and the same systematic analytic strategy was applied.

A second exposure was also investigated: psychological treatment programs provided in prison by the SPPS.¹⁹ Three types of accredited treatment programs were included, mostly introduced and implemented in 2003 and 2004 and commonly used in this sample in group-based settings: general crime prevention programs (eg, cognitive skills, enhanced thinking skills), violence prevention therapies (eg, aggression replacement training, integrated domestic abuse program), and psychological treatments for substance abuse (eg, 12-step program, relapse prevention) (eTable 1 in the Supplement). Treatment program participation was optional but reserved for offenders with medium or high recidivism risk according to the risk principle for effective correctional interventions.²⁰ To be accepted, individuals also had to understand Swedish or English and have at least 2 to 3 months of their sentence remaining. Most programs were translated from original versions in North America or the United Kingdom written by authors from both within and outside correctional services.²¹ Typically, programs are designed to help motivate offenders to change; accept accountability; identify risk factors for their criminal behavior; modify risk factors such as impulsivity, criminal attitudes, and drug craving; and reduce reoffending through relapse prevention plans when they return to society. The programs had all been introduced after recommendation by an accreditation committee of external experts in clinical psychology and treatment research. Treatment integrity was ascertained through instructor supervision of video recordings of actual program sessions. An individual was considered exposed to a treatment program only if the program was completed during the current incarceration period. The unexposed group included those who did not attend or complete the studied treatment programs.

The main outcome was any conviction for violent crime after release, according to the National Crime Register.²² In line with previous work,⁹ violent crime was defined as homicide, assault, robbery, arson, any sexual offense (rape, sexual coercion, child molestation, indecent exposure, or sexual harassment), illegal threats, or intimidation. The date of the crime was the date of the outcome. If no date of the crime was recorded, the conviction date was used instead.

Several covariates were included: age, sex, immigration status (defined as born outside Sweden), sociodemographic factors at the year of release (civil status, highest level of completed education, and disposable income), and criminal history factors (duration of incarceration, violent index offense [the most serious offense that led to the current prison sentence], and any previous violent crime).

For sensitivity analyses, information on lifetime diagnoses of psychiatric disorders was obtained from the National Patient Register, which used the *International Classification of Diseases, Eighth Revision* (ICD-8; 1973-1986, codes 290-315), *ICD-9* (1987-1996, codes 290-319), and *ICD-10* (1997-2009, codes F00-F99).⁶

Statistical Analysis

Cox proportional hazards models were used to calculate hazard ratios (HRs), and medication status was treated as a time-varying covariate in all analyses. Violent reoffending could oc-

cur multiple times during follow-up, with follow-up times reset to 0 after any outcome event.¹⁰ For each medication class, the association with violent reoffending was examined in 2 models. In the first (between-individual) model, rates of violent crime during medicated periods were compared with those in nonmedicated periods after prison release among released prisoners who had received the specific medication at least once during the study period (before, during, or after prison). The analyses were adjusted for age, sex, immigration status, sociodemographic factors, and criminal history covariates, and robust standard errors were calculated to account for correlations between periods for the same individual. The adjusted risk difference was calculated as $I_0 \times (HR_a - 1)$, for which I_0 is the unadjusted event rate in the unexposed group and HR_a is the adjusted HR. Next, stratified Cox regression was used to perform within-individual analyses, with each individual entered as a separate stratum.^{9,10,23} That is, each patient served as his or her own control, and rates of violent reoffending during medicated periods were compared with rates during nonmedicated periods in the same individuals. The within-individual HRs are thus adjusted for confounding by all unmeasured covariates that are constant within each individual during the follow-up (eg, genetic predisposition and all environmental factors at the start of follow-up). Individuals who were invariant with regard to exposure were not excluded, although they did not influence the results of within-individual estimates.

To assess the associations between psychological treatment programs in prison and violent reoffending, HRs were estimated using Cox regression, with adjustment for age, sex, immigration status, sociodemographic factors, and criminological covariates. For each treatment program, rates of violent reoffending were compared between people who completed the treatment program vs those who did not (or never started) in the full cohort. Second, analyses were conducted in subgroups of prisoners to attempt to match programs to their indications in a prespecified analytic plan. For general crime prevention programs, the analysis was performed in prisoners incarcerated for at least 6 months (long enough to complete most programs). For violence prevention, the analysis was conducted in prisoners who were incarcerated for at least 6 months and had a violent index offense. For psychological treatments aimed at substance abuse, the additional analysis was performed in prisoners diagnosed as having substance use disorders.

Several sensitivity analyses were conducted to examine whether results were altered by differences in cohort selection and outcome definition. These analyses were performed only with antipsychotics, psychostimulants, and drugs used in addictive disorders because these medications were found to be significantly associated with reductions in violent reoffending rates. First, the associations were examined in relevant specified diagnostic groups, specifically antipsychotics in prisoners diagnosed as having a schizophrenia spectrum disorder (ICD-8 codes 295, 297, 298.1-9, and 299; ICD-9 codes 295, 297, 298 [except .A], and 299; and ICD-10 codes F20-F29) or bipolar disorder (ICD-8 codes 296.1, 296.3, and 296.8; ICD-9 codes 296A, 296C-296E, and 296W; and ICD-10 codes

Table 1. Baseline and Follow-up Information on All Released Prisoners in Sweden, 2005-2010

Characteristic	No. (%)		
	Full Sample (N = 22 275)	Individuals With Any Psychotropic Medication Dispensed (n = 9915)	Individuals Who Completed Any Psychological Prison Programs (n = 5561)
Person-years at risk	99 851	45 749	25 206
Violent reoffending during follow-up	4031 (18.1)	2097 (21.2)	1103 (19.5)
Male	20 480 (91.9)	8724 (88.0)	5227 (92.3)
Age group, y			
16-25	5547 (24.9)	2086 (21.0)	1654 (29.2)
26-40	7620 (34.2)	3331 (33.6)	2179 (38.5)
>40	9108 (40.9)	4498 (45.4)	1828 (32.3)
Immigration status, born abroad	7506 (33.7)	2668 (26.9)	1607 (28.4)
Highest education, y			
0-9	10 258 (47.6)	4589 (47.1)	2589 (46.3)
10-12	9590 (44.5)	4357 (44.7)	2609 (46.7)
>12	1694 (7.9)	794 (8.2)	388 (7.0)
Unmarried	13 551 (62.9)	5953 (61.1)	3796 (68.0)
Disposable income, median (IQR), US\$ in thousands ^a	11.5 (4.5-18.7)	12.8 (6.3-19.1)	10.0 (4.0-17.6)
Duration of incarceration, mo			
0-6	13 472 (60.5)	6351 (64.0)	1869 (33.0)
7-12	4318 (19.4)	1763 (17.8)	1366 (24.1)
13-24	2815 (12.8)	1180 (11.9)	1433 (25.3)
>24	1634 (7.3)	621 (6.3)	993 (17.5)
Violent index offense ^b	9244 (42.0)	4159 (42.0)	2797 (49.4)
Previous violent crime	14 790 (66.4)	6700 (65.6)	4061 (71.4)

Abbreviation: IQR, interquartile range.

^a After-tax income, including welfare benefits.

^b A violent offense that led to the current prison sentence.

F30-31) before prison release; psychostimulants in prisoners previously diagnosed as having attention-deficit hyperactivity disorder (ADHD) (*ICD-9* code 314; and *ICD-10* code F90); and drugs used in addictive disorders in those previously diagnosed as having substance use disorders (*ICD-8* codes 291, 303, and 304; *ICD-9* codes 291, 292, 303, 304, and 305; and *ICD-10* codes F10-F19). Because of substantial comorbidity,²⁴ antipsychotics were also examined among those with substance use disorders, and drugs used in addictive disorders were also tested among individuals with a schizophrenia spectrum disorder or bipolar disorder. Second, to test whether the associations were different depending on severity of crime, 2 additional outcomes were analyzed: (1) severe interpersonal violence, including homicide and attempted homicide, all forms of assault (including aggravated assault and assault of an officer), rape, sexual coercion, and child molestation²⁵; and (2) any crime (violent and nonviolent crime combined). Third, the associations were tested in those treated before release and those treated only after release. Fourth, the associations were evaluated in those with and without a violent index offense. Fifth, to examine the associations during a longer period after release, follow-up time was extended beyond any reincarceration (when any subsequent time as a convicted or remanded prisoner was excluded). Sixth, as an indirect test of reverse causality, the nonadherence rates of other commonly used medications in those who violently reoffended were examined (eTable 2 in the [Supplement](#)).

All statistical analyses were performed with SAS version 9.4 statistical software (SAS Institute Inc). All tests were 2-sided, and the significance level was set to .05.

Results

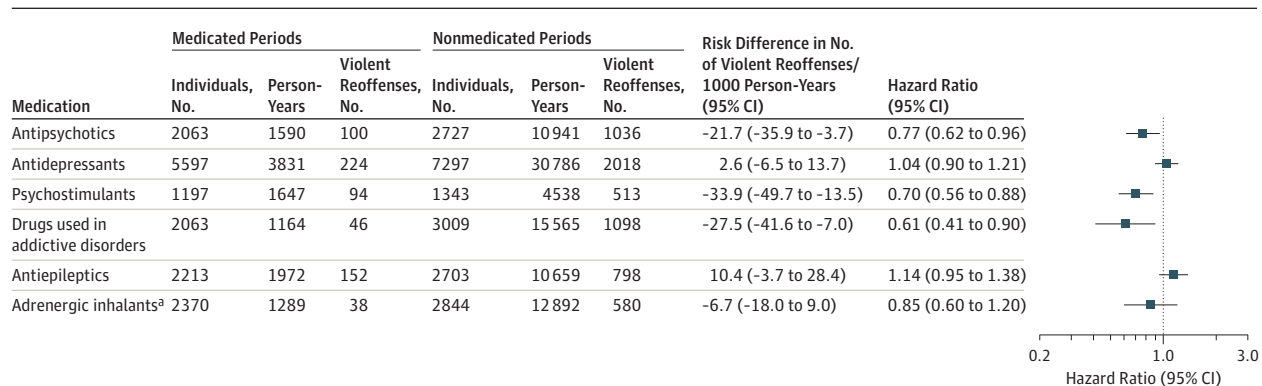
The cohort included 22 275 released prisoners in Sweden (mean [SD] age, 38 [13] years; 91.9% male) from July 1, 2005, to December 31, 2010. **Table 1** shows the baseline sociodemographic and criminal history information of the full cohort of released prisoners (N = 22 275), those with any dispensed psychotropic medications (n = 9915), and those who completed any psychological prison programs (n = 5561). The median follow-up time was 4.6 years (interquartile range, 3.0-6.4 years), and 4031 released prisoners (18.1%) were reconvicted for 5653 violent crimes during follow-up. The use of psychotropic medications after prison release was common; 2085 individuals (9.4%) were dispensed antipsychotics, 5660 (25.4%) antidepressants, 1202 (5.4%) psychostimulants, 2077 (9.3%) drugs used in addictive disorders, and 2235 (10.0%) antiepileptics (the groups were not mutually exclusive; **Table 2**).

In the between-individual analyses, there were 100 violent reoffenses during 1590 person-years of medicated periods with dispensed antipsychotics (a rate of 62.8 per 1000 person-years), whereas there were 1036 violent reoffenses during 10 941 person-years of nonmedicated periods (94.7

Table 2. Dispensed Prescription of Psychotropic and Other Medications Before and After Prison Release Among 22 275 Released Prisoners in Sweden

	No. (%)					
Dispensed Medication	Antipsychotics	Antidepressants	Psychostimulants	Drugs Used in Addictive Disorders	Antiepileptics	Adrenergic Inhalants
Any	2777 (12.5)	7439 (33.4)	1359 (6.1)	3069 (13.8)	2749 (12.3)	2880 (12.9)
Before prison release	1319 (5.9)	4251 (19.1)	431 (1.9)	1631 (7.3)	1140 (5.1)	1411 (6.3)
After prison release	2085 (9.4)	5660 (25.4)	1202 (5.4)	2077 (9.3)	2235 (10.0)	2387 (10.7)

Figure 1. Between-Individual Associations Between Psychotropic Medications and Violent Reoffending Following Prison Release



Hazard ratios were adjusted for age, sex, immigration status, sociodemographic factors, and criminal history covariates. The same individuals could have both medicated and nonmedicated periods. Individuals in the nonmedicated periods included persons who never received medication after prison release, and a

small number of persons in the medicated periods were likely receiving medication the entire duration after release.

^a Adrenergic inhalants were used as a negative control.

per 1000 person-years). The adjusted HR was 0.77 (95% CI, 0.62-0.96), which equated to a risk difference of 21.7 (95% CI, 3.7-35.9) fewer violent reoffenses per 1000 person-years (Figure 1). The adjusted HR associated with dispensed psychostimulants was 0.70 (95% CI, 0.56-0.88), which equated to a risk difference of 33.9 (95% CI, 13.5-49.7) fewer violent reoffenses per 1000 person-years. The adjusted HR associated with dispensed drugs for addictive disorders was 0.61 (95% CI, 0.41-0.90), equating to a risk difference of 27.5 (95% CI, 7.0-41.6) fewer violent reoffenses per 1000 person-years. Other medication classes, including antidepressants (HR = 1.04 [95% CI, 0.90-1.21]), antiepileptics (HR = 1.14 [95% CI, 0.95-1.38]), and adrenergic inhalants (negative control; HR = 0.85 [95% CI, 0.60-1.20]), were not associated with any significant differences in violent reoffending rates. A small number of individuals (175 of 9915 individuals who received any psychotropic medications [1.8%]) had missing values on sociodemographic factors and were excluded from between-individual analyses.

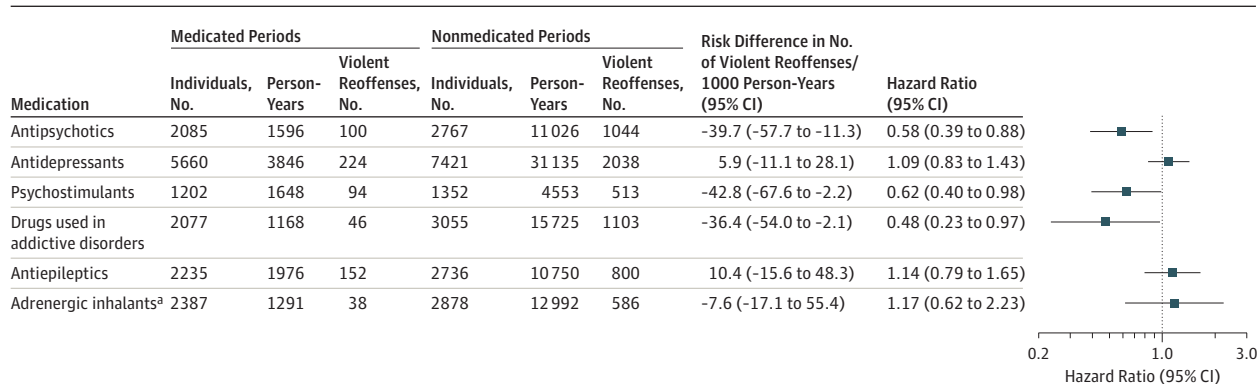
To account for unmeasured confounders that remained constant within each individual during follow-up, rates of violent reoffending were compared in the same individuals during medicated vs nonmedicated periods. The within-individual HR associated with dispensed antipsychotics was 0.58 (95% CI, 0.39-0.88), based on 100 events in 1596 person-years during medicated periods and 1044 events in 11 026 person-years during nonmedicated periods, corresponding to a risk difference of 39.7 (95% CI, 11.3-57.7) fewer

violent reoffenses per 1000 person-years (Figure 2). The within-individual HR associated with dispensed psychostimulants was 0.62 (95% CI, 0.40-0.98), based on 94 events in 1648 person-years during medicated periods and 513 events in 4553 person-years during nonmedicated periods, equating to a risk difference of 42.8 (95% CI, 2.2-67.6) fewer violent reoffenses per 1000 person-years. The within-individual HR associated with dispensed drugs for addictive disorders was 0.48 (95% CI, 0.23-0.97), based on 46 events in 1168 person-years during medicated periods and 1103 events in 15 725 person-years during nonmedicated periods, equating to a risk difference of 36.4 (95% CI, 2.1-54.0) fewer violent reoffenses per 1000 person-years. Again, antidepressants, antiepileptics, and adrenergic inhalants were not associated with any significant differences in violent reoffending rates (HR = 1.09 [95% CI, 0.83-1.43]; 1.14 [95% CI, 0.79-1.65]; and 1.17 [95% CI, 0.62-2.23], respectively).

Psychological Treatments

In the full cohort, completion of psychological general crime prevention programs was associated with a reduced rate of violent reoffending; violence prevention therapies were associated with an increased rate of violent reoffending; and psychological treatments for substance abuse were not associated with violent reoffending (Table 3). In subgroup analyses that matched programs to their indications, the HR associated with general crime prevention programs was 0.77 (95% CI, 0.66-0.90), equating to a risk difference

Figure 2. Within-Individual Associations Between Psychotropic Medications and Violent Reoffending Following Prison Release



The same individuals could have both medicated and nonmedicated periods. Individuals in the nonmedicated periods included persons who never received medication after prison release, and a small number of

persons in the medicated periods were likely receiving medication the entire duration after release.

^a Adrenergic inhalants were used as a negative control.

Table 3. Psychological Treatment Programs Among Prisoners and Violent Reoffending Following Release^a

Treatment Program	Cohort	Exposed Group			Nonexposed Group			Risk Difference in No. of Violent Reoffenses/1000 Person-Years (95% CI)	Hazard Ratio (95% CI)
		Individuals, No.	Person-Years	Violent Reoffenses, No.	Individuals, No.	Person-Years	Violent Reoffenses, No.		
General crime prevention	Full cohort	1157	5568	283	20 385	91 291	5296	-8.6 (-14.8 to -1.4)	0.85 (0.74 to 0.98)
Violence prevention	Full cohort	644	2761	296	20 898	94 097	5283	26.2 (16.0 to 37.8)	1.47 (1.29 to 1.67)
Psychological treatments for substance abuse	Full cohort	2199	9410	550	19 343	87 449	5029	-3.4 (-8.9 to 2.8)	0.94 (0.84 to 1.05)
General crime prevention	Individuals incarcerated for ≥6 mo	1008	4823	212	7537	36 220	1813	-11.6 (-17.1 to -5.1)	0.77 (0.66 to 0.90)
Violence prevention	Individuals incarcerated for ≥6 mo and had a violent index offense	421	1787	197	4032	19 180	1263	5.9 (-12.4 to 30.5)	1.09 (0.81 to 1.46)
Psychological treatments for substance abuse	Individuals diagnosed as having substance use disorder	852	3395	244	5570	22 046	2053	-23.2 (-34.1 to -10.3)	0.75 (0.63 to 0.89)

^a Between-individual analyses, adjusted for age, sex, immigration status, sociodemographic factors, and criminal history covariates.

of 11.6 (95% CI, 5.1-17.1) fewer violent reoffenses per 1000 person-years. The HR associated with psychological treatments for substance abuse was 0.75 (95% CI, 0.63-0.89), for a risk difference of 23.2 (95% CI, 10.3-34.1) fewer violent reoffenses per 1000 person-years. Violence prevention therapies were not significantly associated with violent reoffending. A small number of individuals who had missing values on sociodemographic factors (75 of 5561 individuals [1.3%]) were excluded from the analyses.

Sensitivity Analyses

When examining the effect of psychotropic medications in subgroups of prisoners with diagnosed psychiatric disorders, similar estimates were found for antipsychotics in individuals diagnosed as having a schizophrenia spectrum disorder or bipolar disorder, for psychostimulants in those with ADHD, and for drugs for addictive disorders in those with substance

use disorders (Table 4). Antipsychotics were not associated with lower rates of violent reoffending in those with substance use disorders, whereas drugs used for addictive disorders were linked to substantially less violent reoffending in those with a schizophrenia spectrum disorder or bipolar disorder. The results were largely comparable when outcomes were restricted to severe interpersonal crimes or any crimes (except there was no significant association between drugs used in addictive disorders and rates of any criminal reoffending) (Table 4). A similar pattern of results was found for those treated before release and those treated only after release (Table 4). Similar results were also found when stratifying on index offense or extending the follow-up time to beyond the first reincarceration period (Table 4). For commonly used nonpsychotropic medications, there was higher nonadherence in those who violently reoffended (44.0%) vs those without a violent reoffense (35.7%) (risk difference,

Table 4. Psychotropic Medications and Criminal Reoffending in Released Prisoners by Diagnostic Subgroups, Severity of Outcome, and Duration of Follow-up

Cohort	Outcome Event	Medicated Periods			Nonmedicated Periods			Risk Difference in No. of Violent Reoffenses/1000 Person-Years (95% CI)	Hazard Ratio (95% CI)
		Individuals, No.	Person-Years	Events, No.	Individuals, No.	Person-Years	Events, No.		
Antipsychotics									
Individuals diagnosed as having SSD or BD	Violent crime	361	494	39	759	2646	331	-40.7 (-65.7 to -5.2)	0.67 (0.47 to 0.96)
Individuals diagnosed as having SUD	Violent crime	1179	936	83	6415	24 505	2214	-2.1 (-20.0 to 20.3)	0.98 (0.78 to 1.22)
Full cohort	Severe interpersonal violence	2063	1590	66	2727	10 942	742	-19.1 (-30.2 to -4.7)	0.72 (0.55 to 0.93)
Full cohort	Any crime	2063	1590	662	2727	10 942	6860	-96.5 (-138.0 to -51.4)	0.85 (0.78 to 0.92)
Individuals treated before release	Violent crime	621	747	58	1285	4189	434	-27.1 (-46.2 to -1.5)	0.74 (0.55 to 0.99)
Individuals treated only after release	Violent crime	1442	843	42	1442	6753	602	-33.9 (-49.4 to -12.4)	0.62 (0.45 to 0.86)
Individuals with a violent index crime	Violent crime	951	796	68	1264	4907	669	-35.9 (-59.1 to -5.9)	0.74 (0.57 to 0.96)
Individuals with a nonviolent index crime	Violent crime	1112	794	32	1463	6034	367	-10.5 (-25.9 to 11.6)	0.83 (0.57 to 1.19)
Full cohort with extended follow-up ^a	Violent crime	2649	2023	100	3253	15 418	1344	-25.0 (-37.0 to -10.1)	0.71 (0.58 to 0.88)
Psychostimulants									
Individuals diagnosed as having ADHD	Violent crime	306	450	35	624	1593	286	-57.3 (-94.8 to -3.2)	0.68 (0.47 to 0.98)
Full cohort	Severe interpersonal violence	1197	1647	71	1343	4538	381	-23.6 (-37.6 to -5.6)	0.72 (0.55 to 0.93)
Full cohort	Any crime	1197	1647	699	1343	4538	4047	-258.4 (-308.7 to -203.8)	0.71 (0.65 to 0.77)
Individuals treated before release	Violent crime	273	438	37	419	908	164	-75.6 (-108.3 to -28.1)	0.58 (0.40 to 0.84)
Individuals treated only after release	Violent crime	924	1209	57	924	3630	349	-45.2 (-59.1 to -26.0)	0.53 (0.38 to 0.73)
Individuals with a violent index crime	Violent crime	524	697	57	600	1981	297	-39.7 (-68.0 to -1.8)	0.73 (0.55 to 0.99)
Individuals with a nonviolent index crime	Violent crime	673	950	37	743	2557	216	-29.6 (-46.2 to -5.6)	0.65 (0.45 to 0.93)
Full cohort with extended follow-up ^a	Violent crime	1729	2348	94	1858	7481	813	-41.2 (-54.4 to -24.9)	0.62 (0.50 to 0.77)
Drugs Used in Addictive Disorders									
Individuals diagnosed as having SUD	Violent crime	1534	945	37	6417	24 496	2260	-32.1 (-49.0 to -8.5)	0.65 (0.47 to 0.91)
Individuals diagnosed as having SSD or BD	Violent crime	157	82	1	762	3059	369	-104.5 (-118.4 to -5.7)	0.13 (0.02 to 0.95)
Full cohort	Severe interpersonal violence	2590	1164	31	3499	15 565	750	-18.3 (-27.5 to -5.0)	0.62 (0.43 to 0.90)
Full cohort	Any crime	2590	1164	658	3499	15 565	7270	6.5 (-30.9 to 47.1)	1.01 (0.93 to 1.10)
Individuals treated before release	Violent crime	677	438	14	1586	5612	442	-42.9 (-58.1 to -16.4)	0.46 (0.26 to 0.79)
Individuals treated only after release	Violent crime	1913	725	32	1913	9953	656	-22.9 (-36.1 to -3.8)	0.65 (0.45 to 0.94)
Individuals with a violent index crime	Violent crime	937	301	17	1286	5742	660	-51.2 (-75.6 to -11.6)	0.55 (0.34 to 0.90)
Individuals with a nonviolent index crime	Violent crime	1653	862	29	2213	9823	438	-11.4 (-22.0 to 4.2)	0.74 (0.51 to 1.09)
Full cohort with extended follow-up ^a	Violent crime	3162	1611	46	4000	20 190	1344	-26.1 (-37.3 to -10.4)	0.61 (0.44 to 0.84)

Abbreviations: ADHD, attention-deficit hyperactivity disorder; BD, bipolar disorder; SSD, schizophrenia spectrum disorder; SUD, substance use disorder.

^a Follow-up time was extended beyond any reincarceration (when any subsequent time as a convicted or remanded prisoner was excluded).

8.3% [95% CI, -2.2% to 18.8%]). However, this was not as much as the nonadherence rate for psychotropic medications (57.8% for those with a violent reoffense vs 41.0% for those without a violent reoffense; risk difference, 16.8% [95% CI, 6.2% to 27.3%]) (eTable 2 in the [Supplement](#)).

Discussion

This nationwide longitudinal study of 22 275 released prisoners examined the associations between main classes of psychotropic medication and violent reoffending. Unlike previous work, this investigation used a within-individual design that more carefully accounted for confounding by indication. There were 2 main findings. First, 3 classes of psychotropic medications (antipsychotics, psychostimulants, and drugs used in addictive disorders) were associated with substantial reductions in violent reoffending. Second, the magnitudes of these associations were as strong as and possibly stronger than those for widely disseminated psychological programs in prison.

There has been uncertainty about whether treatment for released prisoners with mental disorders should focus on criminogenic rather than mental health-related factors.²⁶ The current observational study supports the potential role of treating psychiatric disorders, including by antipsychotic medication. The latter is consistent with recent findings that certain psychotic symptoms²⁷ and untreated schizophrenia²⁸ are associated with higher reoffending risk. Further, the findings provide evidence for potential benefits of psychostimulants for prisoners at high risk for reoffending. Although the stability of ADHD from childhood to adulthood is increasingly recognized,^{29,30} ADHD remains commonly underdiagnosed and undertreated in adults, including prisoners.³¹ In relation to substance use disorders, most intervention research in prisoners has focused on psychological treatments.^{32,33} Randomized clinical trials of pharmacological treatments (eg, methadone for opioid dependence) have mostly demonstrated relapse reduction and symptomatic improvement.³⁴ The current study suggests that such benefits may extend to lower rates of violent reoffending if validated in trials. Owing to the high prevalence of substance use disorders among prisoners³⁵ and strong links with premature mortality,³⁶ pharmacological treatments for substance use disorders could have a substantial public health benefit.³⁷

The reduction in violent reoffending was not observed for antidepressants or antiepileptics. Individuals with depression are less violent than individuals with other mental illnesses³⁸; therefore, antidepressants may be less likely than other psychotropic medications to reduce violent reoffending. The finding that antiepileptics were not associated with reduced violent reoffending was unexpected because they can act as mood stabilizers, which are linked with lower rates of violent crime in community settings.⁹ However, previous work also identified important differences by diagnosis; for example, mood stabilizers were associated with violent crime reduction only in bipolar disorder.⁹ Thus, the lack of any association in this study is likely explained by

heterogeneity in their use, including for chronic pain, seizures, and epilepsy.

Secondary analyses demonstrated that completion of psychological treatments targeting general criminal attitudes and substance abuse was associated with reductions in violent reoffending. Further, the associations with these psychological programs were not stronger than those for medications. These findings may have implications for risk management, because prison psychological programs need appropriate facilities, require sufficiently trained and supervised therapists, and are likely to be relatively expensive. Provision of medication after prison release needs evaluation as a possibly cost-effective crime reduction alternative. Because prisoners with psychiatric disorders benefit from both pharmacological and psychological treatments, research should investigate whether combining therapies improves outcomes.³⁹

This study has a number of limitations. Randomized clinical trials in this field are rare owing to feasibility issues, and recruiting, obtaining consent from, and following up participants are considerable logistic challenges. Pharmacoepidemiologic studies offer an alternative approach with large and representative samples.⁹ However, unlike randomized clinical trials, they cannot account for all possible confounders that select individuals to treatment. One approach taken in the current study was to restrict one of the main analyses to individuals who had ever used medications from the studied medication class. Associations were further evaluated by within-individual analyses, an approach that accounted for all confounding factors remaining constant in each individual. Nevertheless, unmeasured time-varying confounding or reverse causality cannot be ruled out. For example, factors that could motivate individuals to use medications may be the same factors that influence them to not reoffend, or some factors that cause persons to resume their violent activities might also lead them to be nonadherent to their medications. These alternative explanations were investigated in secondary analyses. First, the different directions in the associations between different classes of psychotropic medications and violent reoffending would argue against this. If confounding were a major factor, then similar associations between all classes of medications and violent reoffending would be expected. Similarly, if engagement with the health care system was a key explanation, similar reduction across all classes of medication would be expected, which was not demonstrated. Second, no association between adrenergic inhalants (as negative control) and violent reoffending was seen. Third, violent reoffending was associated with higher rates of nonadherence for all categories of medication, but not as much as the nonadherence rate for psychotropic medications. Taken together, it was unlikely that unmeasured confounding or reverse causality could fully explain the observed associations. Nevertheless, observational studies like this one cannot prove causality. Validation with other samples and triangulation with other designs are necessary.

There are other limitations to consider. First, exposure to medication was measured using dispensed prescriptions, which does not account for poor medication adherence. If some

individuals did not use medications as intended, it would bias the results toward null and mean that our findings are likely to be conservative estimates. Second, the data were not sensitive enough to investigate the effects of active symptoms or disease phase.²⁸ Third, the analyses cannot account for all possible confounders that select individuals to prison-based programs. Caution is thus warranted in interpreting these results. Fourth, the findings were based in 1 country. Although Sweden has a low incarceration rate,¹ some key prisoner characteristics are similar to those in other high-income countries (eg, prevalence of psychiatric disorders, reoffending rate, and duration of incarceration).⁶ At the same time, we tested the robustness of the main results and found reduced hazards for violent reoffending in prisoners prescribed antipsychotics, psychostimulants, and drugs used for addictive disorders when we restricted the cohort to individuals who had committed violent offenses on prison entry or prisoners prescribed these medications only after prison release, and we reported similar associations when we extended follow-up beyond first reincarceration.

The absolute numbers of prisoners with psychiatric disorders are large worldwide, and most individuals who could benefit from psychotropic treatment do not receive it after prison release.³⁷ The magnitudes of the associations reported in this study may warrant correctional services to review policies for released prisoners. Evidence-based provision of psychotropic medications to released prisoners may have the potential to make substantial improvements to public health and safety, particularly in countries that are undergoing decarceration.

Conclusions

Among released prisoners in Sweden, rates of violent reoffending were lower during periods when individuals were dispensed antipsychotics, psychostimulants, and drugs for addictive disorders, compared with periods in which they were not dispensed these medications. Further research is needed to understand the causal nature of this association.

ARTICLE INFORMATION

Author Contributions: Drs Chang and Fazel had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Chang, Lichtenstein, Larsson, Fazel.

Acquisition, analysis, or interpretation of data: Chang, Lichtenstein, Långström, Fazel.

Drafting of the manuscript: Chang, Fazel.

Critical revision of the manuscript for important intellectual content: All Authors.

Statistical analysis: Chang.

Administrative, technical, or material support: Lichtenstein, Fazel.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Lichtenstein reported serving as a speaker for Medice. Dr Långström reported serving as national scientific adviser for research and evaluation at the Swedish Prison and Probation Service. Dr Larsson reported receiving grants from Shire and serving as a speaker for Shire and Eli Lilly and Co. Dr Fazel reported receiving a speaker's fee from Janssen. No other disclosures were reported.

Funding/Support: This work was supported by grants from the Wellcome Trust (095806), the Swedish Research Council (2011-2492 and 2013-2280), the Swedish Research Council for Health, Working Life and Welfare (2012-1678 and 2014-2780), the Swedish Initiative for Research on Microdata in the Social and Medical Sciences (340-2013-5867), the European Union Seventh Framework Programme (602768), and the National Institute of Mental Health (1R01MH102221).

Role of the Funder/Sponsor: The sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

REFERENCES

- Walmsley R. World prison population list, 11th ed. http://www.prisonstudies.org/sites/default/files/resources/downloads/world_prison_population_list_11th_edition.pdf. Accessed July 2, 2016.
- Durose MR, Cooper AD, Snyder HN. Recidivism of prisoners released in 30 states in 2005: patterns from 2005 to 2010. <http://www.bjs.gov/content/pub/pdf/rprts05p0510.pdf>. Accessed April 21, 2015.
- Ministry of Justice. Compendium of reoffending statistics and analysis 2012. <https://www.gov.uk/government/statistics/compendium-of-reoffending-statistics-and-analysis>. Accessed April 21, 2015.
- Lamb HR, Weinberger LE. Decarceration of US jails and prisons: where will persons with serious mental illness go? *J Am Acad Psychiatry Law*. 2014; 42(4):489-494.
- McGuire J. A review of effective interventions for reducing aggression and violence. *Philos Trans R Soc Lond B Biol Sci*. 2008;363(1503):2577-2597.
- Chang Z, Larsson H, Lichtenstein P, Fazel S. Psychiatric disorders and violent reoffending: a national cohort study of convicted prisoners in Sweden. *Lancet Psychiatry*. 2015;2(10):891-900.
- Fazel S, Seewald K. Severe mental illness in 33,588 prisoners worldwide: systematic review and meta-regression analysis. *Br J Psychiatry*. 2012; 200(5):364-373.
- Leucht S, Tardy M, Komossa K, et al. Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis. *Lancet*. 2012;379(9831):2063-2071.
- Fazel S, Zetterqvist J, Larsson H, Långström N, Lichtenstein P. Antipsychotics, mood stabilisers, and risk of violent crime. *Lancet*. 2014;384(9949):1206-1214.
- Lichtenstein P, Halldner L, Zetterqvist J, et al. Medication for attention deficit-hyperactivity disorder and criminality. *N Engl J Med*. 2012;367(21):2006-2014.
- Frankle W, Shera D, Berger-Hershkovitz H, et al. Clozapine-associated reduction in arrest rates of psychotic patients with criminal histories. *Am J Psychiatry*. 2001;158(2):270-274.
- Dailey LF, Townsend SW, Dysken MW, Kuskowski MA. Recidivism in medication-noncompliant serious juvenile offenders with bipolar disorder. *J Clin Psychiatry*. 2005;66(4):477-484.
- McMurrin M. What works in substance misuse treatments for offenders? *Crim Behav Ment Health*. 2007;17(4):225-233.
- Gibbons RD, Amatya AK, Brown CH, et al. Post-approval drug safety surveillance. *Annu Rev Public Health*. 2010;31:419-437.
- Bulloch AG, Patten SB. Non-adherence with psychotropic medications in the general population. *Soc Psychiatry Psychiatr Epidemiol*. 2010;45(1):47-56.
- Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, Ekblom A. The Swedish personal identity number: possibilities and pitfalls in healthcare and medical research. *Eur J Epidemiol*. 2009;24(11):659-667.
- Kriminalvården. The Swedish Prison and Probation Service website. <https://www.kriminalvarden.se/>. Accessed April 21, 2015.
- Wettermark B, Hammar N, Foré CM, et al. The new Swedish Prescribed Drug Register—opportunities for pharmacoepidemiological research and experience from the first six months. *Pharmacoepidemiol Drug Saf*. 2007;16(7):726-735.
- Kriminalvården. Behandlingsprogram. <http://www.kriminalvarden.se/behandling-och-vard/behandlingsprogram>. Accessed October 30, 2014.
- Andrews DA, Bonta J. *The Psychology of Criminal Conduct*. 5th ed. London, England: Routledge; 2010.
- Correctional Service Canada. Offender rehabilitation: correctional programs. <http://www.csc-scc.gc.ca/correctional-process/002001-2001-eng.shtml>. Accessed October 30, 2014.

22. National Council for Crime Prevention. *Kriminalstatistik 2010*. Västerås, Sweden: National Council for Crime Prevention; 2011.
23. Chang Z, Lichtenstein P, D'Onofrio BM, Sjölander A, Larsson H. Serious transport accidents in adults with attention-deficit/hyperactivity disorder and the effect of medication: a population-based study. *JAMA Psychiatry*. 2014;71(3):319-325.
24. Webb RT, Lichtenstein P, Larsson H, Geddes JR, Fazel S. Suicide, hospital-presenting suicide attempts, and criminality in bipolar disorder: examination of risk for multiple adverse outcomes. *J Clin Psychiatry*. 2014;75(8):e809-e816.
25. Fazel S, Långström N, Hjern A, Grann M, Lichtenstein P. Schizophrenia, substance abuse, and violent crime. *JAMA*. 2009;301(19):2016-2023.
26. Skeem JL, Manchak S, Peterson JK. Correctional policy for offenders with mental illness: creating a new paradigm for recidivism reduction. *Law Hum Behav*. 2011;35(2):110-126.
27. Coid JW, Ullrich S, Kallis C, et al. The relationship between delusions and violence: findings from the East London First Episode Psychosis Study. *JAMA Psychiatry*. 2013;70(5):465-471.
28. Keers R, Ullrich S, Destavola BL, Coid JW. Association of violence with emergence of persecutory delusions in untreated schizophrenia. *Am J Psychiatry*. 2014;171(3):332-339.
29. Chang Z, Lichtenstein P, Asherson PJ, Larsson H. Developmental twin study of attention problems: high heritabilities throughout development. *JAMA Psychiatry*. 2013;70(3):311-318.
30. Polanczyk G, Rohde LA. Epidemiology of attention-deficit/hyperactivity disorder across the lifespan. *Curr Opin Psychiatry*. 2007;20(4):386-392.
31. Ginsberg Y, Quintero J, Anand E, Casillas M, Upadhyaya HP. Underdiagnosis of attention-deficit/hyperactivity disorder in adult patients: a review of the literature. *Prim Care Companion CNS Disord*. 2014;16(3):PCC.13r01600.
32. Pearson FS, Lipton DS. A meta-analytic review of the effectiveness of corrections-based treatments for drug abuse. *Prison J*. 1999;79(4):384-410. doi:10.1177/0032885599079004003
33. Mitchell O, Wilson DB, MacKenzie DL. Does incarceration-based drug treatment reduce recidivism? a meta-analytic synthesis of the research. *J Exp Criminol*. 2007;3(4):353-375. doi:10.1007/s11292-007-9040-2
34. Rich JD, McKenzie M, Larney S, et al. Methadone continuation versus forced withdrawal on incarceration in a combined US prison and jail: a randomised, open-label trial. *Lancet*. 2015;386(9991):350-359.
35. Fazel S, Bains P, Doll H. Substance abuse and dependence in prisoners: a systematic review. *Addiction*. 2006;101(2):181-191.
36. Binswanger IA, Stern MF, Deyo RA, et al. Release from prison—a high risk of death for former inmates. *N Engl J Med*. 2007;356(2):157-165.
37. Chandler RK, Fletcher BW, Volkow ND. Treating drug abuse and addiction in the criminal justice system: improving public health and safety. *JAMA*. 2009;301(2):183-190.
38. Brennan PA, Mednick SA, Hodgins S. Major mental disorders and criminal violence in a Danish birth cohort. *Arch Gen Psychiatry*. 2000;57(5):494-500.
39. Huhn M, Tardy M, Spineli LM, et al. Efficacy of pharmacotherapy and psychotherapy for adult psychiatric disorders: a systematic overview of meta-analyses. *JAMA Psychiatry*. 2014;71(6):706-715.