

Clozapine's Effect on Recidivism Among Offenders with Mental Disorders

Mansfield Mela, MSc, and Gu Depiang, PhD

Mental disorder is associated with criminal reoffending, especially violent acts of offending. Features of mental disorder, psychosocial stresses, substance use disorder, and personality disorder combine to increase the risk of criminal recidivism. Clozapine, an atypical antipsychotic, is indicated in the treatment of patients with psychotic disorders. This article is the report of a community follow-up study of a matched control of those treated with clozapine ($n = 41$) and those treated with other antipsychotics ($n = 21$). Rates of reoffending behavior in the general, nonviolent, violent, and sexual categories were calculated after two years of follow-up. Although not statistically significant, the two-year criminal conviction rates of those treated with other antipsychotics in all offense categories except sexual reoffending were two-fold higher than in those treated with clozapine. The time from release to the first offense and crime-free time in the community were significantly longer in the clozapine group. By prolonging the time it takes from release to first offense, clozapine confers additional crime-reduction advantages.

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Among those with mental illness, the severity of mental disorder and its manifestations, substance use,¹ and the threat–control override symptoms of psychosis² increase the likelihood of criminal reoffending. Nonadherence to medications and substance use signaled a higher risk for violent behavior in a study involving 331 subjects with major mental illness.³ Attempts to disrupt the link between mental disorder and criminal activity have produced various models of treatment of those with mental illness, especially among resistant patients or those who are difficult to treat. Cross-sectional⁴ and retrospective and prospective⁵ cohort studies have demonstrated that those with mental disorder, whether in prison,⁶ hospitals, or the community,⁷ commit more violent offenses. For public safety therefore, it has further been suggested that treatment of psychotic disorders should improve symptoms and reduce violent behav-

ior.⁶ Various treatment paradigms have been studied to reduce the almost 10 percent risk of violence attributable to psychotic disorders, especially in an individual with schizophrenia.⁸ The assertive community treatment and intensive case management models of treating high-need and high-risk patients with mental disorders and offenders have received mixed reviews of their effectiveness in reducing criminal activity.^{9,10} In a community sample of more than 700 patients randomly assigned to an intensive case management and a control standard care arm, no significant reduction in violence was demonstrated.¹¹

Regarding offenders with mental disorders, there is a dearth of studies examining the mechanism of violent behaviors and the methods of reducing them. Adequate treatment is expected to lead, not only to improved symptoms, but to reduction of behavioral manifestations that contribute to criminal offending. Violence risk factors in the population of offenders with mental disorders include substance use disorder, psychosocial stressors, family history of criminality, and other factors associated with violence in offenders without mental disorders. In-reach teams and modified intensive care for offenders with mental disorders have also been reported to have mixed

Mansfield Mela is Associate Professor of Psychiatry, University of Saskatchewan, Saskatoon, Saskatchewan, Canada. Dr. Gu Depiang is Research Associate, Correctional Services of Canada, Regional Psychiatric Centre, Saskatoon, Saskatchewan, Canada. Presented at the 44th annual meeting of the American Academy of Psychiatry and the Law, October 23–27, 2013, San Diego, CA. Address correspondence to: Mansfield Mela, MSc Psych, University of Saskatchewan, 103 Hospital Drive, Saskatoon, S7N 0W8, Saskatchewan, Canada. E-mail: mansfieldmela@gmail.com

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results. For instance the forensic assertive community treatment was effective among nonviolent offenders in a randomized control trial. The cost of the treatment, however, was higher than for those in standard treatment.^{9,10}

Clozapine has been associated with significant reduction of positive, negative, suicidal, and cognitive symptoms, including improvement in employability and institutional adjustment.^{12,13} It goes without saying that the indications for clozapine have expanded over the years to include those that are not based solely on pharmacological mechanism of action. The effectiveness of clozapine recognizes that monitoring is included in the care of those prescribed it.¹² Studies of offenders on clozapine have had various objectives and outcomes. Among a small number of offenders with mental disorders in a forensic psychiatric hospital, a significant number of those treated showed reduction in level of security, improvement in manifestation of aggressiveness, and enhanced tolerability.¹³ In another study, the first 50 patients on clozapine in a maximum-security psychiatric hospital were followed up for two years. Compliant clozapine users demonstrated improved rates of discharge from hospital and symptom reduction. Those who discontinued clozapine had worse outcomes.¹⁴ Clozapine was found to reduce violence and symptoms of psychosis and to improve functioning. Offenders with mental disorders who are on clozapine showed improved functioning and better adjustment in a secure hospital compared with those not on clozapine.¹² These studies were helpful in examining the outcomes within the secure hospitals but not where the risk-reduction benefit may be more practical and useful, in the community. They also were not control studies.

We sought to examine the effect of clozapine on criminal reoffending in offenders with mental disorders who are released into the community. We hypothesized that those treated with clozapine would remain in the community longer and commit fewer and less severe offenses than those not treated with clozapine.

Method

The subjects were offenders with mental disorders treated at the Regional Psychiatric Center (RPC) in Saskatoon, one of five psychiatric hospitals in Canada, where those serving a federal sentence are admitted to receive treatment. The sentences were of more

than two years' duration and were for more serious offenses, especially violent ones. The University of Saskatchewan Research ethics board and the national headquarters of the Correctional Service of Canada approved the study. Our initial analysis of outcomes within the treatment facility described the process of inclusion. This study was of a naturalistic design and included those with a final diagnosis of a psychotic disorder confirmed independently by two research psychiatrists.¹²

All 65 patients treated with clozapine for more than 6 weeks were included in the treatment (clozapine group) arm of the study. Patients in the clozapine treatment group were selected after being treated consecutively for six weeks from the initiation of clozapine. This time frame was chosen to reflect the likely period by which commitment to the medication would have been confirmed. By that time, the patients would have completed several tests for blood level of the drug, would have experienced immediate side effects of the medication, and would have been titrated to a therapeutic dose. Thirty-three remaining patients with diagnoses of psychotic disorders and treated with other antipsychotics formed the nonclozapine, control arm of the study. Thus, the initial sample was made up of 98 patients: 65 in the clozapine group and 33 in the nonclozapine group. The control arm was matched with the experimental arm for age, gender, and offense severity. The characteristic demographic and clinical features of the study population and the outcome within the institution have been described.¹²

By November 17, 2012, the data collection date (DCD), 63 percent of the 98 patients had had a follow-up time of more than two years after release. We used the Canadian Police Information Centre (CPIC), a national database of all charges and convictions to track down the offense histories in the community after release of 62 offenders with mental disorders (41 in the clozapine group and 21 in the nonclozapine (control) group). The latter group was selected to include those who were treated only with other atypical or typical antipsychotics.¹² The control group excluded anyone who had been on clozapine for more than two weeks. Those in the clozapine group had to have been on the medication for at least six weeks. The CPIC data identify the time or date of first-offense conviction after release, and those are further divided into four categories or type of offense: nonviolent, violent, sexual, and any offenses. The

CPIC also gives the number of convictions for each offender once in the database. The percentage of offenders convicted within each category is then calculated. All 98 offenders were in the database, and information on offense convictions, except for deceased offenders, was obtained for statistical analysis.

The incident relative risk was calculated for all the offenses and compared between the two treatment groups. The rates of reconviction of the four categories (any, nonviolent only, violent only, and sexual offenses only) were compared by using Fisher's exact test. The results took into account all offenses that occurred during the follow-up period, but concentrated on those occurring during the two years of postdischarge monitoring after the data were first collected, given that some offenders may revolve in and out of the penal system.

We conducted a survival analysis (time to first offense after release) of the two groups along the four offense categories. The mean survival times, in months after release from the RPC, were compared between the clozapine and the nonclozapine groups, up to the data collection date (DCD). The Wilcoxon test was used for overall comparison. The mean differences (and confidence intervals) in time from release to first reconviction between the two groups were also calculated.

Results

The demographic and clinical variables and results of matching between the two groups have been reported.¹² The CPIC DCD was November 17, 2012. Five patients from the clozapine group (7.7%) and three from the nonclozapine group (9.1%) were deceased. There was no statistically significant difference between the deceased patients in the two groups. Sixty-two (63.3%) of the initial 98 offenders with mental disorders had been released into the community. The percentages of release persons from the two groups (clozapine, 63.1%; nonclozapine, 63.6%) were the same. The tables show the rates of reconviction in the different offense categories. Table 1 refers to all convictions from the day of release and Table 2 to convictions within two years of release.

The mean times in months from release to the first reconviction that fell into the four offense categories were all longer in the clozapine than in the nonclozapine group (Table 3).

The clozapine group had a mean period from release to the DCD of 125 months compared with the

Table 1 Reconviction Rates for Four Offense Categories Comparing the Study Groups Throughout the Period of Follow-up

Categories of Reconviction	Clozapine (n = 41)	Nonclozapine (n = 21)	Fisher's Exact Test P
Any/all offenses	21 (51.2)	11 (52.4)	0.572
Nonviolent	19 (46.3)	9 (42.9)	0.505
Violent	13 (31.7)	7 (33.3)	0.558
Sexual	8 (19.5)	2 (9.5)	0.265

Data are the number (percentage of group).

nonclozapine group, with a mean period of 73 months. The mean difference in period since release of the clozapine group was significantly longer (by 51.6 months) than that of the nonclozapine group (independent *t* test = 4.834, *df* = 60; *p* < .000).

Figures 1–4 are the survival analysis curves of the clozapine versus the nonclozapine group. They depict a longer survival for the clozapine group until the first conviction (Fig. 1) and similar survival curves for the two medication groups for time from release to the first nonviolent conviction (Fig. 2).

Discussion

The clozapine group had a lower, albeit not significantly different, incidence of all of the categories of reoffending, except sexual. It also conferred a significantly longer duration between release and first offense. These results are better appreciated when the length of follow-up, two years in this study, is matched for both groups. For instance the clozapine group had essentially half the violent offense reconviction rate of the nonclozapine group. The clozapine group showed a longer survival curve and period, especially for violent recidivism. It is tempting to invoke the superior symptom reduction qualities of clozapine over the other nonclozapine medications used by the participants. Although the improvement in positive, negative, and cognitive symptoms potentially affects the pattern of reoffending, it is likely that other features contribute equally or more relevantly in keeping clozapine-treated patients

Table 2 Reconviction Rates for Four Offense Categories Comparing the Study Groups With a 2-Year Follow-up Period

Categories of Reconviction	Clozapine (n = 41)	Nonclozapine (n = 21)	Fisher's Exact Test p
Any/all offenses	10 (24.4)	9 (42.9)	0.115
Nonviolent	10 (24.4)	6 (28.6)	0.474
Violent	5 (12.2)	6 (28.6)	0.108
Sexual	4 (9.8)	1 (4.8)	0.444

Data are the number (percentage of group).

Table 3 Mean Difference Between the Date of Release and the Date of First Reconviction for All Categories

Offense Category	Clozapine – Nonclozapine (months)	Confidence Interval
Any reconviction	10.2	–5.4 to 25.9
Nonviolent	7.05	–7.7 to 21.9
Violent	21.3	–4.9 to 47.6
Sexual	8.6	–15.2 to 32.3

from reoffending in comparison to the patients treated with other antipsychotics. Clozapine has been associated with a reduction in violent and aggressive behaviors, even in the absence of significant reduction in psychotic symptoms.¹² In a randomized controlled study, clozapine demonstrated antiaggressive properties in comparison to olanzapine and haloperidol.¹⁵ Evidence from a recent systematic review of all studies looking at this antiaggression property has provided significant support to this finding.¹⁶ This feature can directly impact and reduce violent reoffending. Clozapine has been portrayed to have specific antihostility properties based on its distinct mechanism of concurrently decreasing (5-HT2 antagonism) and enhancing (5-HT1B) serotonergic transmission.¹² Clozapine’s affinity is higher for dopamine D4 receptors than for dopamine D2 receptors. The ratio is higher than one and is considered

relevant in mediating clozapine’s antiaggression property.¹⁷ In this study, violent reoffending was delayed by 21 months and halved at the 2-year follow-up. This result is in comparison to that in individuals with similar psychotic and violence risk but treated with other antipsychotic medications. In a slightly different study design, similar and lower arrests rates (32.6%) of clozapine-treated patients in a large sample of community patients was found, which is consistent with our finding.¹⁸ In that this is the same study population in which inpatient hospital outcomes were shown to be positive, it is also possible that such improvement carried over upon release to the community.¹² This finding is consistent with the results in another study showing that stability in the hospital translates easily to compliance and, indirectly, to safety in the community.¹⁹

Patients treated with clozapine are, on the whole, more likely to be connected with the medical system. They require blood monitoring and timely contact with a health professional. This regular contact was initially thought to be an explanation for the effectiveness of clozapine and to enhance socio-occupational functioning in the community among patients with resistant schizophrenia.^{20,21} This form of active monitoring and support and the effect of clozapine on reducing substance use are likely to contribute to

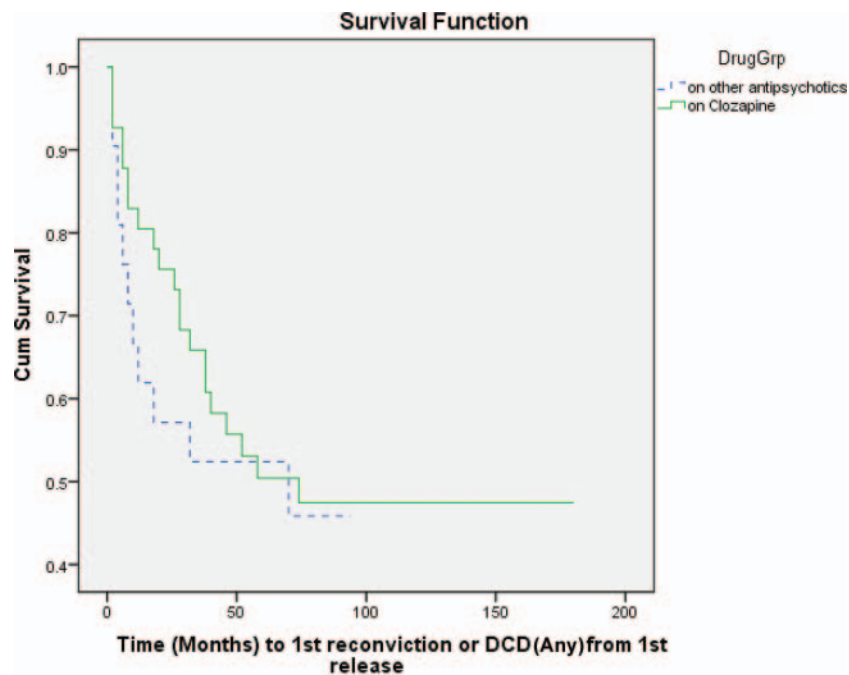


Figure 1. Survival analysis curves showing the decline in the nonclozapine group compared with the clozapine group. From the DCD, the clozapine group had a longer period in the community upon release before the first conviction.

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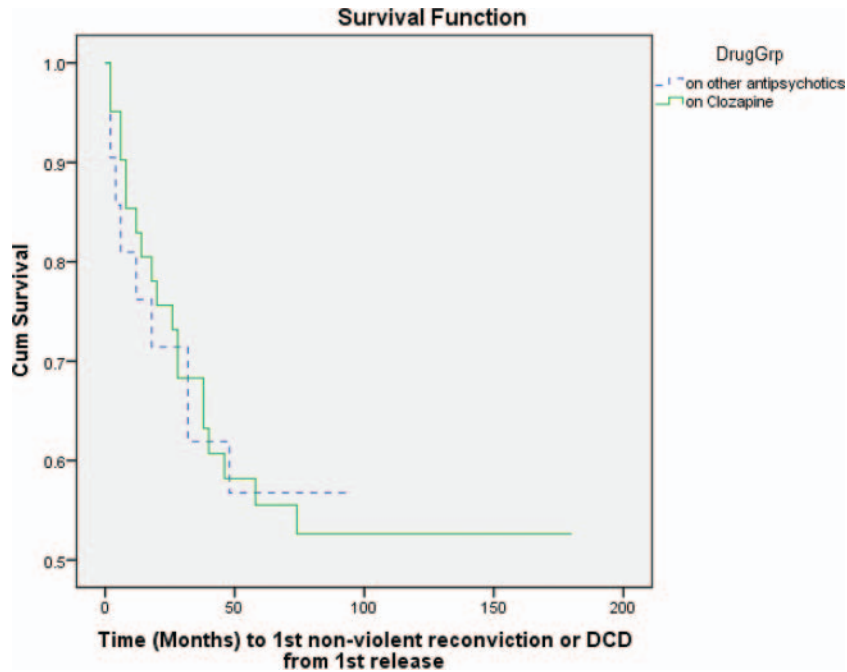


Figure 2. Survival curves for the two medication groups showing time in months from first release date to DCD or date of first nonviolent conviction.

reductions in reoffending.²² By reducing one of the most significant risk-elevating factors of substance use, clozapine can contribute to reduced recidivism, as we found in our study. Clozapine requires some level of compliance to be successfully administered. It advertently selects more compliant individuals and

may enhance their prosocial behavior and thus contribute to the positive outcomes we observed.

We did not monitor the regularity of health care contact in the patients released and thus are unable to state whether clozapine-treated patients had more contact with those in the health professions. We as-

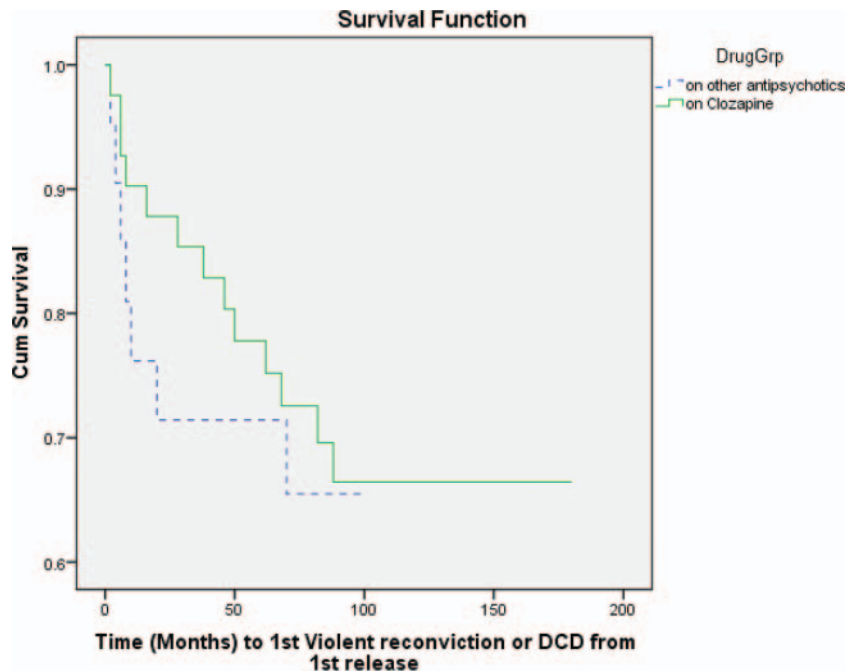


Figure 3. Survival curves for clozapine showing a longer time interval between the release date and the DCD or first conviction for a violent act.

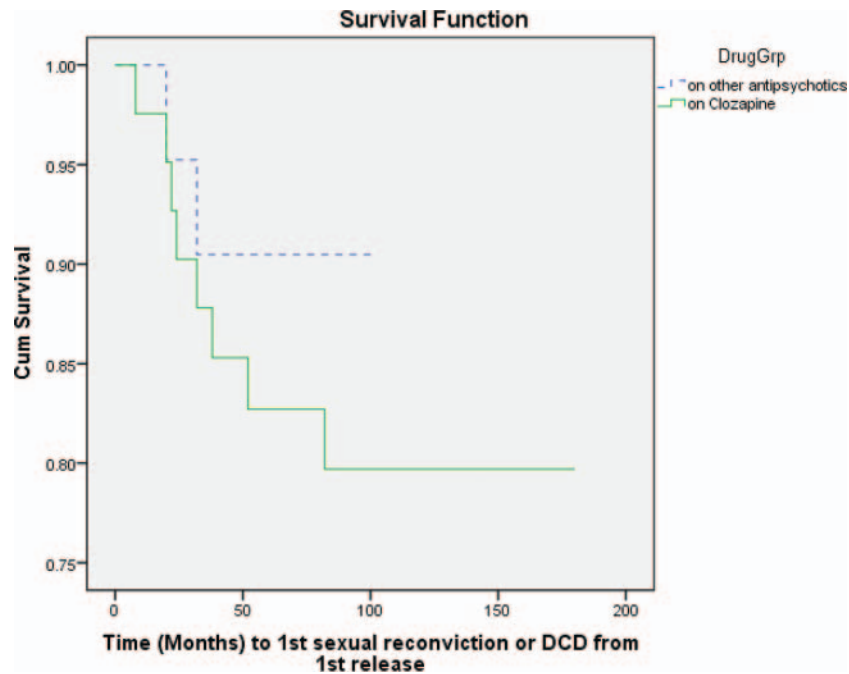


Figure 4. Survival curves for clozapine showing shorter time interval than other medications between the release date and the DCD or first conviction for a sex crime.

sume that they did and estimate that any behavioral or symptomatic deterioration was likely to be detected and adequately managed. If those not treated with clozapine are not encouraged or forced to have regular contact with mental health services, they would not be expected to attend regular appointments, and reducing their risk of recidivism through early detection and intervention would not be possible. The higher rate, albeit not statistically significant, of offending behavior, violent and nonviolent, could flow out of this lack of monitoring and supervision. There is evidence that monitoring offenders and supervising them ensures safety in the community and possibly reduces criminal recidivism.^{9,10} The principles of intensive case management that allow regular contact with offenders with high risk ensures similar monitoring for patients on clozapine. Such improvement is similar to the paradigm in those taking depot antipsychotic injections, who are shown to have a lower relapse rate than those on oral medication.^{23,24} It is also likely that those on clozapine will be less apt to use illicit substances, and that they will be engaged in addressing, through contact with mental health care professionals, other social and risk-elevating factors. It is expected that they will be directed to the correct sources of housing, employment, and social assistance. They are more likely

to receive such guidance if they are in contact with mental health professionals, an advantage of registration with a clozapine-monitoring system with its link to the mental health system.

The longer duration between release and reconviction and the length of crime-free period among those treated with clozapine is testimony to the long-term stability provided by a comprehensive treatment based on biopsychosocial models. It suggests that those high-risk offenders with psychosis should be considered for enrollment to receive clozapine treatment.^{16,18,19} It also suggests that supervision akin to clozapine monitoring could be instituted in those offenders in the community, even if they are not being treated with clozapine. This type of supervision adopts a care-based approach and guarantees regular contact with health care professionals who monitor and support offenders with mental disorders with problem-solving and skills training.²⁵ Non-pharmacological benefits, such as more regular contact with health care staff, psychological interventions, or support from family and caregivers, have been proposed as the likely mediating factors for effective reduction of violence in those compliant with medication.²⁶ The offenders with mental disorders treated with the other antipsychotics were statistically similar to those treated with clozapine in rate of

reoffending and reconviction. This similarity is supported by a recent pharmacoepidemiological study that found treatment with antipsychotics, mood stabilizers, and clozapine all to be protective against violent crime.²⁶ Also the benefit of treatment before release from the treatment center, possibly resulting in better compliance and correction of risk-potentiating features, could have contributed to the former's successful outcome.^{12,14,27} The similarity in nonviolent outcome between clozapine and other antipsychotic prescriptions was noted to be consistent with the finding in over 82,000 individuals prescribed medications in the study by Fazel and colleagues.²⁶ In that study, the prescription of medication (clozapine, other antipsychotics, and mood stabilizers) was associated with similar reductions in any crime, drug-related crime, less severe crime, and suspected violent crime, including significant reductions associated with clozapine for all outcomes except drug-related crime.²⁶

The higher, though not statistically significant, rate of sexual reoffending in the clozapine group may be related to the nonselection process of the study participants. If there were more sex offenders in the clozapine group, it is expected that sexual reoffending would be higher among them. Clozapine is indicated for use among those with the most severe psychopathologies and those likely resistant to other treatments. Such a risk level may be different for sexual reoffending. There is no direct relationship of the use of clozapine and specific reduction of sexual offending behavior. Clozapine is used in treating aggressive patients with schizophrenia.²⁸ It may have the benefit of reducing the general aggression but not necessarily the paraphilia, which can increase sexual recidivism by inducing sexual offending. Although clozapine, similar to other psychotropic medications, is known to have sexual side effects, it has yet to show demonstrable efficacy in reducing sexual offending behavior. The overall benefit of the clozapine in this population of offenders may well be directed at patients likely to have a long history of criminal and mental health system involvement as well as versatile criminal offenders.

These findings are encouraging for the mental disorder component in recidivism. Most risk assessment studies recognize the role of major mental and substance use disorders in potentiating risk of violent and nonviolent offending. By targeting these symptoms and improving functionality,^{12,14} clozapine

may play a larger role in risk reduction among offenders with mental disorders. Such reduction of criminal acts is consistent with findings of institutional criminal behavior among the same and similar samples.^{12,14} The findings are in line with studies among nonoffenders^{18,19} and offenders alike.^{13,27} Future studies are needed to identify those for whom clozapine is indicated and useful for risk reduction.

We note that some studies point to the lack of efficacy of psychotropic medications in reducing criminal activity.^{29,30} Thus, further study is needed, with control for the other psychosocial risk factors and observation of the effect on both charges and conviction. We chose criminal conviction for our study, to ensure the validity of the behavior. Many patients with mental disorder are easily arrested and rearrested over minor offenses.^{31,32} This means of selection and excluding the use of charges cannot be said to have changed the findings either way, given that the two groups were not significantly different, except in the length of time the clozapine group remained crime free. Equally, the protective effect of clozapine lasted longer than that of the other antipsychotics. The specific benefit of clozapine may wane over the longer follow-up time as other non-pharmacological risk factors become more relevant. Two years after release, estimation of supervised outcome for all offenders by the correctional system has been adopted to assist in standardization of results. The longer the follow-up time, the less the difference in effective risk-reducing measures.³³ Compliance with clozapine, retention of skills developed while in treatment, and effective regulatory supervision are more likely to end in two years than later. Clinically meaningful services were said to dwindle one year after release in a study of offenders with mental disorders.³⁴

A limitation of this study is that it was not a double-blind control study and it did not account for other factors associated with criminal recidivism.³⁵ It was not determined whether inpatients on clozapine continued to have contact with health professionals and to use clozapine for the whole period of the follow-up. Since treatment is usually voluntary in the community, some patients may have stopped their medication. This limitation also applies to the group on other antipsychotics. Ensuring adherence to prescribed medication and estimating its actual use are problems, even in randomized controlled trials where analyses are based on dispensed medications.

To estimate compliance, investigators used the initial 45 days of the prescription as evidence, similar to our six-week limit on taking clozapine.²⁶

The participants in this study were selected while they were inpatients of a treatment center. Not many were on depot injections, and we were unable to compare outcomes in the two groups. Such a comparison would be relevant, especially with the recent finding that confirmed the role of depot injections in the largest study of violence and antipsychotics yet.²⁶ Another limitation is that the outcome depended on administrative data through the CPIC and was based on criminal conviction, not reoffending, or other behavioral indicators. There are advantages, as the data were collected blind to the goals of the study, but these must be viewed in light of the disadvantages of not collecting clinical and other relevant psychosocial factors.

Notwithstanding these limitations, we have shown that in line with the theories of an anti-aggressive property, clozapine prescription in offenders with mental disorders for which clozapine is indicated should be regarded as a risk-reducing strategy. In those with mental disorders who do not qualify to be prescribed clozapine, knowledge on how compliance, monitoring, and supervision are ensured in those treated with clozapine should be transferable lessons. Reducing violent behavior and crime are important interpersonal and public outcomes.

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