Bipolar Disorder and Violent Crime

New Evidence From Population-Based Longitudinal Studies and Systematic Review

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Context: Although bipolar disorder is associated with various adverse health outcomes, the relationship with violent crime is uncertain.

Objectives: To determine the risk of violent crime in bipolar disorder and to contextualize the findings with a systematic review.

Design: Longitudinal investigations using general population and unaffected sibling control individuals.


Participants: Individuals with 2 or more discharge diagnoses of bipolar disorder (n=3743), general population controls (n=37,429), and unaffected full siblings of individuals with bipolar disorder (n=4059).

Main Outcome Measure: Violent crime (actions resulting in convictions for homicide, assault, robbery, arson, any sexual offense, illegal threats, or intimidation).

Results: During follow-up, 314 individuals with bipolar disorder (8.4%) committed violent crime compared with 1312 general population controls (3.5%) (adjusted odds ratio, 2.3; 95% confidence interval, 2.0-2.6). The risk was mostly confined to patients with substance abuse comorbidity (adjusted odds ratio, 6.4; 95% confidence interval, 5.1-8.1). The risk increase was minimal in patients without substance abuse comorbidity (adjusted odds ratio, 1.3; 95% confidence interval, 1.0-1.5), which was further attenuated when unaffected full siblings of individuals with bipolar disorder were used as controls (1.1; 0.7-1.6). We found no differences in rates of violent crime by clinical subgroups (manic vs depressive or psychotic vs nonpsychotic). The systematic review identified 8 previous studies (n=6383), with high heterogeneity between studies. Odds ratio for violence risk ranged from 2 to 9.

Conclusion: Although current guidelines for the management of individuals with bipolar disorder do not recommend routine risk assessment for violence, this assertion may need review in patients with comorbid substance abuse.

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familial confounding, we studied rates of violent crime in individuals with bipolar disorder compared with their unaffected siblings. Fourth, to contextualize our findings, we conducted a systematic review and meta-analysis of research on bipolar disorder and violence, which to our knowledge is the first quantitative synthesis of the available evidence.

METHODS

NEW EMPIRICAL INVESTIGATION AND STUDY SETTING

We linked the following nationwide population-based registries in Sweden: the Hospital Discharge Registry (HDR [National Board of Health and Welfare]), the National Crime Register (National Council for Crime Prevention), the national censuses from 1970 and 1990 (Statistics Sweden), and the Multi-Generation Register (Statistics Sweden). In Sweden, all residents (including immigrants) have a unique 10-digit personal identification number that is used in all national registers, enabling the linking of data in these registers.

PATIENTS WITH BIPOLAR DISORDER

Using the HDR, which includes all individuals admitted to and discharged from any hospital for assessment or treatment (including forensic psychiatric hospitals and the few private providers of inpatient health care), we identified as case individuals those who fulfilled 2 criteria. First, they had to have been discharged from hospitals between January 1, 1973, and December 31, 2004, and to have had discharge diagnoses of bipolar disorder on at least 2 separate occasions according to the International Classification of Diseases, Eighth Revision (ICD-8) (1973-1986 [diagnostic codes 296.1, 296.3, and 296.88]), ICD-9 (1973-1996 [codes 296A, 296C-296E, and 296W]), or ICD-10 (1997 onward [codes F30 and F31]). All hospitalized individuals receive ICD diagnoses on discharge. Second, cases were born between January 1, 1958, and January 1, 1989, so that they were at least aged 15 years (the age of criminal responsibility) at the start of the study on January 1, 1973. We required that bipolar disorder had been diagnosed on at least 2 separate occasions to increase diagnostic precision; this stipulation should minimize false-positive diagnoses by excluding individuals with only 1 diagnostic opinion.

Data were also extracted for every individual with regard to discharges between January 1, 1973, and December 31, 2004, with principal or comorbid diagnoses of alcohol abuse or dependence (ICD-8 code 303, ICD-9 codes 303 and 303.1, and ICD-10 code F10 except x.5) and drug abuse or dependence (ICD-8 code 304, ICD-9 codes 304 and 303.9, and ICD-10 codes F11-F19 except x.3). This information was used as a marker for comorbid alcohol or drug abuse disorders.

DIAGNOSTIC VALIDITY AND RELIABILITY

In the HDR, there is good evidence for distinguishing between diagnoses of schizophrenia and those of nonschizophrenia psychoses based on record review and interview using the OPCRIT computerized diagnostic system to generate DSM-IV diagnoses.13 Only approximately 1% of individuals discharged from the hospital have missing personal identification numbers.14 More than 90% of individuals with severe mental illness are thought to be admitted over any given 10-year period in Sweden.15 Since January 1, 1973, the HDR has recorded national coverage for psychiatric disorders. Consequently, the register has been widely used in psychiatric epidemiologic investigations.16 In 2008, 2 board-certified psychiatrists (including N.L.) conducted a review of the medical records of 135 randomly chosen patients with 2 separate HDR diagnoses of bipolar disorder in 1 Swedish county. This analysis yielded an agreement rate of 91.5%; most false-positive diagnoses were severe chronic unipolar depressive disorders (usually with comorbid substance abuse or nonbipolar psychosis) but without the distinct hypomanic or manic episodes needed to diagnose bipolar disorder (data available from the authors). A prior validity study17 found fair agreement between substance abuse diagnoses in the HDR and a comprehensive 4-week inpatient assessment used as the criterion standard. Results of a more recent larger comparison study18 suggested fair to moderate agreement specifically for comorbid substance abuse in schizophrenia (κ statistic [SE], 0.37 [0.23]; P < .001; corresponding to 68% full agreement).

We investigated 2 overlapping samples of individuals with bipolar disorder. The first was a national sample of those with 2 or more hospital diagnoses of bipolar disorder (n = 3743). The second, a subgroup of the first sample, comprised all individuals with 2 or more hospital diagnoses of bipolar disorder who also had full siblings unaffected by bipolar disorder (n = 2570). We identified 2 comparison groups who had never been hospitalized for bipolar disorder at any time during the study period. The first was a random selection of approximately 10 individuals in the general population matched on birth year and sex for each individual with bipolar disorder (37429 general population control individuals matched to 3743 patients with bipolar disorder). The second comprised unaffected full siblings of individuals with bipolar disorder (4059 full-sibling controls and 2570 individuals with bipolar disorder), unmatched by age or sex and identified using the Multi-Generation Register.19 The Multi-Generation Register records each person born in Sweden from 1933 onward and ever registered as living in Sweden from 1960 onward, matched to their parents.20 For immigrants, similar information exists for those who moved to Sweden before age 18 years together with 1 or both parents. Both comparison groups included individuals who may have had a substance abuse history; individuals with only 1 hospitalization for bipolar disorder were not included in the comparison groups.

OUTCOME MEASURES

Data on all convictions for violent crime from January 1, 1973, until December 31, 2004, were retrieved for all individuals aged 15 years (the age of criminal responsibility in Sweden) and older. In keeping with other studies,14,16 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. Attempted and aggravated forms of offenses, where applicable, were also included. Convictions were used because the Swedish Criminal Code11 determines that individuals are convicted regardless of mental illness. These included verdicts of not guilty by reason of insanity, noncustodial sentences, fines and cautions, and transfers to forensic hospitals. No plea bargaining is permitted. The crime register has excellent coverage; only 0.05% violent crimes had missing associated personal identification numbers between 1988 and 2000.14

SOCIODEMOGRAPHIC COVARIATES

Data on civil status and income were gathered from the 1970 and 1990 national censuses. For income, if there were no 1990 census data, we used 1970 data and converted these to the 1990 monetary value. Income was then divided into tertiles (low, medium, and high) for the purpose of further analysis. When data
on individual income were missing, we used the household income (also divided into tertiles) of the family of origin at the time of the 1970 or 1990 census. Single marital status was defined as being unmarried, divorced, or widowed (but included those who were cohabiting). Immigrant status was defined as being born outside of Sweden or having at least 1 parent born outside of Sweden. In the main analyses, missing data were not replaced by imputation or other methods.

MAIN ANALYSES

We estimated the association between bipolar disorder and violent crime with conditional logistic regression analysis, as per related work using matched or sibling controls via the clogit command in STATA software version 10 (StataCorp LP, College Station, Texas). The clogit command fits conditional (fixed effects) logistic regression models to matched case-control groups. Only violent crime after the second inpatient diagnosis of bipolar disorder was included in the analyses. Approximately 10 controls from the general population were selected for each case. In the sibling control study, all unaffected siblings were compared with each individual having bipolar disorder. Age and sex were matched or adjusted for in all analyses. In the general population study, controls were matched by birth year and sex. In the sibling control investigation, we adjusted for sex and age in analyses involving full-sibling comparisons by calculating the age difference (in years) between patient and sibling. We tested possible confounders (income, marital status, and immigrant status) by examining whether they were each independently associated with case status and violent crime at $P < .05$ using $\chi^2$ tests in univariate analyses. Income and marital status (being single vs nonsingle) met these criteria and were included as covariates in adjusted models. Immigrant status was a confounder in the general population comparison. Because substance abuse may be on the causal pathway between bipolar disorder and violent crime, we did not include it as a confounder; instead, stratum-specific estimates are provided. In building the regression model, all significant confounders were entered simultaneously with bipolar disorder status as exposure and with violent crime as outcome.

SUBGROUP ANALYSES

We performed several within-group comparisons of individuals with ICD-9 or ICD-10 diagnoses of bipolar disorder (which was not possible using ICD-8 because of poorer subtype classification) based on their last diagnosis. First, we compared individuals diagnosed as having a manic episode ($n=925$) (ICD-9 codes 296A-296C and ICD-10 codes F301, F308, F309, and F311) with those diagnosed as having a depressive episode ($n=461$) (ICD-9 code 296D and ICD-10 codes F313 and F314). Second, we compared individuals having any manic, mixed, or hypomanic episode ($n=1224$) (ICD-9 codes 296A, 296C, and 296E and ICD-10 codes F300, F301, F308, F309, F311, and F316) with those having a depressive episode ($n=961$). Third, using ICD-10 diagnoses only (which was not possible using ICD-8 and ICD-9 because of poorer subtype classification), we compared individuals diagnosed as having a psychotic episode ($n=403$) (ICD-10 codes F302, F312, and F315) with those having a nonpsychotic episode ($n=923$) (ICD-10 codes F300, F301, and F308-F311 and codes 313, 314, 316, and 317). For the subgroup analyses, binary logistic regression was used, and adjustments were made for age, sex, income, and marital status. A further subgroup analysis was performed in which we recalculated risk estimates by assigning an extra category to missing income and marital status information so that the model included all cases and controls.

SYSTEMATIC REVIEW AND META-ANALYSIS

Computerized MEDLINE, EMBASE, and PsyCINFO searches were performed for studies published from January 1, 1970, to February 1, 2009, using a combination of the terms violent crime, bipolar, psychosocial, and psychot. References were retrieved and hand searched for other citations, including gray literature (unpublished or semiofficially published); non-English-language publications were translated. To supplement the search, US National Criminal Justice Reference Abstracts and an extensive bibliography on crime and mental disorder prepared for the Health Agency of Canada were searched. When required, we contacted authors of studies for additional information. For the National Survey on Drug Use and Health, we extracted bipolar data directly from the authors' Web site for 2002 because the published data have pooled diagnoses. Our inclusion criteria comprised case-control studies (including cross-sectional surveys) and cohort studies, which allowed an estimation of the risk of violence in patients with bipolar disorder compared with a general population comparison group.

A standardized form was used to extract data, including information on study design, geographic location of the study, last year of follow-up for violence (“study period”), diagnostic criteria, definition of violence, method of violence ascertainment, sample size, mean age, and any adjustment for sociodemographic factors. Suitability for inclusion was assessed, and data extraction was conducted independently by 2 of us (S.F. and N.L.); any differences were resolved by discussion among coauthors. Meta-analysis of violent outcomes risk was performed, generating pooled odds ratios (ORs) with 95% confidence intervals (CIs) for random-effects models. Such an approach weights studies more equally and is considered more appropriate for meta-analyses with substantial heterogeneity. Heterogeneity among studies was estimated using Cochran Q (reported with a $\chi^2$ value and $P$ value) and the $I^2$ statistic, with the latter describing the percentage of variation across studies that is owing to heterogeneity rather than chance. The $I^2$ statistic, unlike Cochran Q, does not inherently depend on the number of studies considered, with values of 25%, 50%, and 75% taken to indicate low, moderate, and high levels of heterogeneity, respectively. Analyses were performed with STATA software, version 10.

The Regional Ethics Committee at the Karolinska Institutet approved the study. The protocol was recorded as 2005/174-31/4.

NEW LONGITUDINAL STUDIES

Basic sociodemographic information and substance abuse comorbidity among individuals with bipolar disorder and among general population and full-sibling controls are given in Table 1. The age at diagnosis is older than the age at violent crime because it applies to the whole sample with bipolar disorder and not just the subgroup convicted of offenses (violent crime will usually be skewed to younger groups).

The prevalence of convictions for violent crime among individuals with bipolar disorder was 8.4%, while the rate was 3.5% in general population controls and 6.2% in unaffected full siblings ($P < .05$ for comparison of rates for the whole group having bipolar disorder with general population controls and for the subgroup having bipolar disorder and their siblings unaffected by bipolar dis-
order [Table 2]). Therefore, there was an increased risk of violent crime among the individuals with bipolar disorder: the adjusted OR (aOR) was 2.3 (95% CI, 2.0-2.6) for their risk of violent crime compared with that of general population controls. The risk increase was reduced to an aOR of 1.6 (95% CI, 1.2-2.1) when individuals with bipolar disorder were compared with their siblings unaffected by bipolar disorder.

The risk of violent crime among patients having bipolar disorder and substance abuse comorbidity was more than 21.3% and was significantly higher than the risk among patients without such comorbidity (Table 3). Therefore, compared with general population controls, the odds of violent crime among those having bipolar disorder and substance abuse comorbidity was 6.4 (95% CI, 5.1-8.1); compared with unaffected siblings, the risk was also high but was attenuated (aOR, 2.8; 95% CI, 1.8-4.3). In contrast, for patients having bipolar disorder without substance abuse comorbidity, the risk of violent crime was minimally elevated (aOR, 1.3; 95% CI, 1.0-1.5) compared with that in the general population and was not significantly elevated compared with that in unaffected siblings (aOR, 1.1; 95% CI, 0.7-1.6). Although in the latter comparison the rate of violent crime was slightly higher among the unaffected siblings, the relative risk was not higher because the risk estimate accounted for matching and adjustments.

The rate of violent crime was also calculated among the general population and unaffected siblings with hospital discharge diagnoses of substance abuse. Among the general population, the rate was 33.0% (95% CI, 31.2%-34.8%), and among the unaffected siblings it was 41.5% (95% CI, 35.5%-47.5%).

**SUBGROUP ANALYSES**

We found no evidence of manic episodes being specifically associated with increased risk of violence compared with depressive episodes (aOR, 1.2; 95% CI, 0.8-1.9) nor for manic, mixed, or hypomanic episodes vs depressive episodes (1.1; 0.7-1.7) nor for psychotic vs nonpsychotic bipolar disorder episodes (0.8; 0.4-1.4). When stratified by substance abuse comorbidity, these risk estimates were unchanged (data not shown); for example, there was no increased risk when individuals having manic episodes and comorbidity were compared with individuals having depressive episodes and comorbidity. When individuals with missing information on in-

### Table 2. Risk of Violent Crime in Individuals Having Bipolar Disorder Followed Up Longitudinally Compared With Unaffected General Population Control Individuals and Unaffected Full-Sibling Controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Individuals With Bipolar Disorder</td>
<td>Unaffected General Population Control Individuals</td>
</tr>
<tr>
<td>Age at diagnosis, mean (SD), y</td>
<td>28.5 (7.1)</td>
<td>NA</td>
</tr>
<tr>
<td>Age at first violent crime, mean (SD), y</td>
<td>26.8 (7.5)</td>
<td>24.0 (7.2)</td>
</tr>
<tr>
<td>Male sex, No. (%)</td>
<td>2108 (56.3)</td>
<td>21080 (56.3)</td>
</tr>
<tr>
<td>Individual annual income, 1000 SEK, mean (SD)</td>
<td>80.4 (60.5)</td>
<td>102.3 (66.4)</td>
</tr>
<tr>
<td>Single status, No. (%)</td>
<td>2672 (84.1)</td>
<td>22281 (74.8)</td>
</tr>
<tr>
<td>Substance abuse comorbidity, No. (%)</td>
<td>795 (21.2)</td>
<td>694 (1.9)</td>
</tr>
</tbody>
</table>

**Abbreviations:** NA, not applicable; SEK, Swedish krona.

- **a** Determined at the time of the 1990 census.
- **b** Divorced, widowed, not married, cohabiting.
- **c** Proportion with any inpatient discharge for drug or alcohol abuse or dependence between January 1, 1973, and December 31, 2004.

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**Table 1. Sociodemographic Information and Substance Abuse Comorbidity Among Individuals in 2 Longitudinal Studies of Bipolar Disorder and Violent Crime in Sweden**

<table>
<thead>
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<th>Variable</th>
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</tbody>
</table>
come and marital status were included in the overall model, the aOR was 2.4 (95% CI, 2.1-2.7) for violent crime among individuals with bipolar disorder compared with general population controls.

We also investigated differences by sex. The rate of violent crime was higher among men; of individuals with bipolar disorder, 226 of 1635 men (13.8%) and 88 of 2108 women (4.2%) had been convicted of a violent offense. However, compared with rates of violent crime among general population controls of the same sex, women with bipolar disorder had a higher risk of violent crime (aOR, 4.1; 95% CI, 3.0-5.5) than men with bipolar disorder (1.9; 1.6-2.3).

SYSTEMATIC REVIEW

We identified 8 previous studies that reported on risk of violence in individuals with bipolar disorder compared with general population controls. Five were conducted in the United States (2458 cases with bipolar disorder) and 1 each in New Zealand (n = 19), Israel (n = 81), and Switzerland (n = 82). Different outcome measures were used, including a combination of crime registers, combined register-based and self-report instruments, and self-report methods.

We included the first of the new Swedish studies reported herein (individuals with bipolar disorder compared with general population controls, who were matched by age and sex but not adjusted for other confounders, to be consistent with the other studies) with these 8 previous investigations to conduct a meta-analysis (Figure). When synthesizing the data, in individuals with bipolar disorder, 625 of 6383 (9.8%) had violent outcomes compared with 3346 of 112,944 (3.0%) in the general population comparisons. The ORs ranged from 2.2 to 8.9, and the pooled random-effects crude OR was 4.1 (95% CI, 2.9-5.8), with high heterogeneity between studies ($I^2 = 87.2\%$).

This longitudinal study of 3743 individuals with bipolar disorder has 2 main findings. First, there was an increased risk for violent crime among individuals with bipolar disorder. Most of the excess violent crime was associated with substance abuse comorbidity. Second, there was an increased risk for violent crime among the unaffected siblings of individuals with bipolar disorder. This finding further weakens the relationship between

<p>| Table 3. Risk of Violent Crime in Individuals Having Bipolar Disorder With and Without Substance Abuse Comorbidity Followed Up Longitudinally Compared With Unaffected General Population Control Individuals and Unaffected Full-Sibling Controls |
|---------------------------------|---------------------------------|---------------------------------|</p>
<table>
<thead>
<tr>
<th>Control Group</th>
<th>Adjusted Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bipolar Disorder Without Substance Abuse Comorbidity</td>
<td>Bipolar Disorder With Substance Abuse Comorbidity</td>
</tr>
<tr>
<td>Matched Unaffected Controls</td>
<td>Matched Unaffected Controls</td>
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<td>--------------------------------</td>
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</tr>
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<td>Unaffected general population controls</td>
<td>1.3 (1.0-1.5)</td>
</tr>
<tr>
<td>Unaffected full-sibling controls</td>
<td>1.1 (0.7-1.6)</td>
</tr>
</tbody>
</table>

$^a$ Violent crime was defined as actions resulting in convictions for homicide, assault, robbery, arson, any sexual offense, illegal threats, or intimidation.

$^b$ General population controls were matched by age (birth year) and sex, and the association was adjusted by income (lowest vs middle and highest tertiles), marital status (single vs nonsingle), and immigrant status (individual or at least 1 parent born outside of Sweden). Unaffected full-sibling controls were not matched, but the comparison was adjusted for age, sex, income, and marital status.

|$P<001$)
bipolar disorder per se and violent crime and highlights the contribution of genetic or early environmental factors in families with bipolar disorder.

The systematic review and meta-analysis herein provide some context for these findings. The increased risk estimates varied from 2 to 9, with a pooled OR of 4.1 (95% CI, 2.9-5.8) using a random-effects model. This pooled OR is higher than that in the present study for 2 principal reasons. First, the pooled estimate is mostly based on crude estimates rather than adjusted estimates, as many previous studies have not fully or even partially adjusted for socioeconomic confounders. Second, unlike most previous studies, we only examined violent crime after diagnosis of bipolar disorder, which is a likely explanation for the lower risk estimate in our study. In a meta-regression analysis of schizophrenia and violence investigations, this study characteristic also explained lower risk estimates.

Bipolar disease severity (measured by the presence of psychotic symptoms) or diagnostic subgroups (manic vs depressive episode) were not associated with a violent crime risk increase in our study. Instead, the association between bipolar disorder and violent crime seemed to be largely mediated by substance abuse comorbidity. The risk increase in patients with bipolar disorder and substance abuse comorbidity was more than that found in a related study of schizophrenia. In the present study, the OR for violent crime in patients with substance abuse comorbidity was 6.4 (95% CI, 5.1-8.1). In schizophrenia, the risk increase in patients having comorbidity was 4.2 (95% CI, 3.9-5.0). Other work has found mediation of substance abuse in patients with bipolar disorder. Although we found that the rate of violent crime was 4.2% in women with bipolar disorder and 13.8% in men with bipolar disorder, the relative risk in women compared with that in female general population controls was higher than the corresponding estimate in men. Sex differences in violence have also been reported for severe mental illness.

Available data suggest a common familial etiology for bipolar disorder, violent criminality, and substance abuse. First, we found that the risk of violent crime in individuals with bipolar disorder was confined to those with comorbid substance use, and among those with substance abuse comorbidity, the risk was reduced from 6.4 relative to that of general population controls to 2.8 in comparison to sibling controls, indicating that familial effects are important for the association between violent crime and bipolar disorder among individuals with substance abuse. Second, comorbidity between bipolar I disorder and substance misuse is high (60% in the National Comorbidity Survey Replication), and in our data familial effects confounded the association between bipolar disorder and substance abuse (unaffected siblings had twice the rate of substance abuse [4.0%] compared with that of general population controls [1.9%]). Third, related work from Sweden demonstrated a 5-fold increased risk of violent crime in individuals with substance abuse; hence, substance abuse seems to be a likely explanation for increased violence in the unaffected siblings. The finding of shared familial etiology for bipolar disorder, violent criminality, and substance abuse is consistent with at least 2 likely explanations for the increased risk of violence among some patients with bipolar disorder. Bipolar disorder (with a predominantly genetic cause) may lead to substance abuse, which in turn increases the risk for violent crime. Alternatively, there may be a shared genetic susceptibility to substance abuse, bipolar disorder, and violent crime. However, with the available data, it is not possible to disentangle these 2 explanations, nor the relative genetic and environmental causes for the familiality. Further work is required to better understand the mechanisms (eg, by obtaining information on individuals who commenced violent crime before the onset of bipolar disorder).

Two implications follow from the role of comorbidity in mediating violent crime among individuals with bipolar disorder. First, detection is important, and current practice guidelines highlight the fact that comorbidity may be overlooked. Second, substance abuse treatment for individuals with bipolar disorder is likely to reduce the risk for violence and other adverse outcomes (including suicide). However, more trial evidence is required. A recent expert consensus statement identified a single trial, that of psychoeducation, for the treatment of comorbidity in patients with bipolar disorder. Other recommendations include the involvement of an addiction psychiatrist and the potential value of dual-diagnosis treatment programs.

Although the overall risk estimate is similar to that found in schizophrenia investigations, we found no increased violence risk in patients having bipolar disorder without substance abuse comorbidity, whereas in schizophrenia a small risk increase remained. Current UK guidelines for bipolar disorder discuss the importance of assessing substance abuse but do not discuss the risk of violence. According to US guidelines, clinical experience suggests that violence may be present in some patients with bipolar disorder, but guidelines do not recommend routine risk assessment or quantification of the risk. Furthermore, they state that comorbid psychosis may contribute to this risk, which is not confirmed by the present data, although it is possible that different mechanisms (including psychotic motives) are relevant for more severe crimes such as murder. What evidence-based recommendations for assessment of risk for violent crime should be made for patients with bipolar disorder, given our findings? Since the risk estimate for bipolar disorder with substance abuse comorbidity is similar to that for substance abuse alone (reported to increase the risk of violence between 6- and 7-fold in a recent review), we suggest that detailed assessment is appropriate for all individuals with substance abuse, irrespective of bipolar diagnosis.

The strengths of the present empirical work include the large number of violent offenders with bipolar disorder compared with other studies included in the meta-analysis, more than all previous studies combined. In addition, we only included violent crime after diagnosis of bipolar disorder, reducing the possibility that the reported association is confounded by conviction precipitating hospital admission among those with bipolar disorder. We also made careful adjustment for possible sociodemographic confounders. We accounted for cohort effects by matching for year of birth, and we ad-
justed for residual confounding using unaffected siblings as controls.

Study limitations include our reliance on hospital data for case ascertainment and comorbidity. By relying on hospitalization data, the mean age at onset of illness in our sample was 27 years, which is older than is usually found in prospective and retrospective reviews of patient data. The actual age at onset of illness will have been earlier because of our reliance on hospitalization data. The rates of violence that we reported might have been higher if we had included a younger sample of patients before hospital diagnosis. However, this would not affect relative risk estimates because cases and controls were matched on age.

Over a 30-year period, the vast majority of individuals (>90%) in Sweden with severe mental illness were likely to have been hospitalized at some point. This means that some individuals with mental illness were missed by these registers, and this weighted our findings to those with more severe bipolar disorder presentations, some of whom were admitted because of violence risk or actual violent incidents. Such biases would have tended to overestimate the risk, although charges may have been dropped by the police in some cases.

We used 2 diagnoses of bipolar disorder for study inclusion; hence, some individuals with bipolar disease were missed. Whether these individuals differ in their rates of violent crime is uncertain. No difference was found in a study of schizophrenia that compared rates of violent crime in cohorts of patients having 2 diagnoses vs those having 1 diagnosis, and this pattern may be similar in bipolar disorder. A further limitation is that information on comorbidity is likely specific, as it is based on hospital diagnoses, but is not particularly sensitive, so it is possible that the effects of substance abuse have been underestimated. Furthermore, the sensitivity of register-based data for the controls is likely to be worse than that for the patients, among whom inpatient admissions allow for the assessment of substance abuse comorbidity; hence, any comparison between individuals with substance abuse in the general population and patients must be made with caution. Information on other potentially important comorbidities, such as childhood conduct problems, was not available. Although we relied on conviction data, other work has shown that the degree of underestimation of violence is similar in psychiatric patients and controls compared with self-report measures; hence, the risk estimates were not affected. A recent systematic review examining the relationship between schizophrenia and violence also found no difference in risk estimates between self-report and register-based studies.

Rates of violent crime and their resolution are similar across western Europe, and assault rates are comparable between Sweden and the United States, suggesting the potential generalizability of our findings. In addition, alcohol sales per capita in Sweden are similar to those in the United States, although comparative information on illegal drug use is limited. Furthermore, Sweden is similar to the United States in terms of an internationally recognized proxy for psychiatric morbidity, namely, age-adjusted disability-adjusted life-years. Prevalences of mental disorders differ minimally across European countries, with a median prevalence of 0.9% for bipolar disorder, which compares with 1.0% in a recent US epidemiologic survey. A final limitation is that our results do not clarify whether any particular clinical phase of bipolar disorder (such as mania) may increase the risk of violent crime or whether there are potential roles of treatment and medication nonadherence in mediating this risk. Interview-based prospective studies, perhaps as part of a large simple trial, will be necessary to clarify these issues.

In summary, we used complementary designs to investigate the risk of violent crime in patients with bipolar disorder and included a meta-analysis of all available studies. Our empirical work substantially increases the evidence base by including more individuals with bipolar disorder than the previous studies combined and more precise methods to handle confounding. We demonstrated a clear association of bipolar disorder with violent crime in individuals with substance abuse comorbidity. The risk associated with a bipolar diagnosis per se appears low; it was minimal compared with that in general population controls when there was no comorbid substance abuse, and there was no association when violence risk in patients was compared with that in unaffected siblings. Our findings suggest the need for violence risk assessment and management in patients with bipolar disorder who have substance abuse comorbidity.

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