

A National Study of Violent Behavior in Persons With Schizophrenia

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Context: Violent behavior is uncommon, yet problematic, among schizophrenia patients. The complex effects of clinical, interpersonal, and social-environmental risk factors for violence in this population are poorly understood.

Objective: To examine the prevalence and correlates of violence among schizophrenia patients living in the community by developing multivariable statistical models to assess the net effects of psychotic symptoms and other risk factors for minor and serious violence.

Design: A total of 1410 schizophrenia patients were clinically assessed and interviewed about violent behavior in the past 6 months. Data comprise baseline assessments of patients enrolled in the National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness.

Setting and Patients: Adult patients diagnosed as having schizophrenia were enrolled from 56 sites in the United States, including academic medical centers and community providers.

Main Outcome Measures: Violence was classified at 2 severity levels: minor violence, corresponding to simple

assault without injury or weapon use; and serious violence, corresponding to assault resulting in injury or involving use of a lethal weapon, threat with a lethal weapon in hand, or sexual assault. A composite measure of any violence was also analyzed.

Results: The 6-month prevalence of any violence was 19.1%, with 3.6% of participants reporting serious violent behavior. Distinct, but overlapping, sets of risk factors were associated with minor and serious violence. "Positive" psychotic symptoms, such as persecutory ideation, increased the risk of minor and serious violence, while "negative" psychotic symptoms, such as social withdrawal, lowered the risk of serious violence. Minor violence was associated with co-occurring substance abuse and interpersonal and social factors. Serious violence was associated with psychotic and depressive symptoms, childhood conduct problems, and victimization.

Conclusions: Particular clusters of symptoms may increase or decrease violence risk in schizophrenia patients. Violence risk assessment and management in community-based treatment should focus on combinations of clinical and nonclinical risk factors.

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HOW COMMON IS VIOLENT behavior in people with schizophrenia under different conditions? Is violence in this population mainly due to psychopathological features or other common risk factors? To what extent is violence associated with developmental and life-historical variables that precede the onset of schizophrenia? Definitive answers to these questions remain elusive. Meanwhile, clinicians who treat schizophrenia patients in the community are increasingly expected (even legally obligated) to assess and manage the risk of violence in those under their care.^{1,2}

Research studies³ fall short of providing useful predictive or explanatory models of community violence specific to schizo-

phrenia; it is a daunting challenge to measure rare, but diverse, events linked to a disease that is also uncommon—affecting less than 1% of the population. Baseline data from the National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)⁴ project, a national study investigating the cost-effectiveness of antipsychotic medications, provide an unprecedented opportunity to gain a fine-grained and clinically useful understanding of the occurrence of community violence in patients with schizophrenia.

No single variable explains violence in schizophrenia; rather, violent behavior occurs within a social-ecological system, involving a "whole person" with a particular life history and state of health or disease,

interacting with a particular social surround.^{5,6} Epidemiological studies³ in the general population have found violent behavior to be associated with younger age, male sex, lower socioeconomic status, and substance abuse. We assess violence risk in schizophrenia patients by examining the net contribution of variables in 5 domains: dispositional factors (demographic characteristics and socioeconomic position), social-contextual factors (household composition, social contact, and social support), life-historical factors (childhood victimization and childhood conduct problems), clinical factors (current symptoms, impairment, and functioning), and treatment factors (hospitalization and institutional contact).

Within this multivariable framework, we focus most specifically on the clinical domain and the nature of the (much-debated) link between violence and psychotic symptoms.⁷⁻¹⁷ The CATIE project provides significant new evidence in this area, overcoming some key methodological shortcomings of previous studies and offering several advantages, including a large sample of schizophrenia patients, a highly specific measure of violent behavior, and comprehensive clinical assessments. To our knowledge, it is the first study to examine the main effects of, and interactions between, “positive” and “negative” schizophrenia symptoms in association with violence in the community.

Our central research questions are as follows: (1) How strong is the net association between psychotic symptoms and community violence in schizophrenia patients in usual-care settings, taking into account the potential joint effects of other variables, including dispositional, social-contextual, life-historical, clinical, and treatment factors? (2) How do explanatory models of serious and minor violent behavior in these patients differ? We examine these questions using a multivariate analysis of a national sample of persons with schizophrenia (N = 1410).

METHODS

STUDY DESIGN AND SAMPLE CHARACTERISTICS

The data come from the National Institute of Mental Health CATIE project. The CATIE project was approved by local institutional review boards, and participants gave written informed consent. Details of the study design and methods were previously described in detail.⁴ Specifically, the CATIE project is a randomized trial conducted between January 1, 2001, and December 4, 2004, at 57 clinical sites in 24 states throughout the United States (16 university clinics, 10 state mental health agencies, 7 Veterans' Affairs Medical Centers, 6 private nonprofit centers, 4 private practice sites, and 14 mixed-system sites). Reflecting the urban concentration of the US population (73% reside in large metropolitan counties, US Census Bureau data), 69% of the selected CATIE study sites were located in metropolitan areas with more than 1 000 000 persons; 24% were in medium metropolitan areas, with populations between 250 000 and 1 000 000; and the remaining 8% were in less populated counties, including some nonmetropolitan and rural vicinities (percentages do not total 100 because of rounding). These sites were located in 48 cities and towns, representing every region of the United States, except Alaska. The clinical sites are

typical of the real-life settings in which people with schizophrenia receive treatment in the United States.

Study sites systematically screened inpatients and outpatients for eligibility for the study. Individuals were considered appropriate for referral to the study if they were assessed to have adequate decision-making capacity and their antipsychotic treatment was deemed suboptimal because of either efficacy or tolerability concerns.

Formal sample inclusion criteria were broad: aged 18 to 65 years; currently meets or has met in the past *DSM-IV* diagnostic criteria for schizophrenia, based on the Structured Clinical Interview for Axes I and II *DSM-IV* Disorders—Patient Edition¹⁸; review of clinical records and input from available informants (with review and consensus on most plausible diagnosis when sources disagreed); has a condition judged appropriate for treatment with an oral medication; demonstrates adequate decisional capacity to make a choice about participating in the research study; and provides informed consent to participate.

Patients were excluded if they were in their first episode of schizophrenia; had a diagnosis of schizoaffective disorder, mental retardation, or other cognitive disorder; had past serious adverse reactions to any of the proposed treatments; had a history of treatment resistance, defined by persistence of severe symptoms despite adequate trials of one of the proposed treatments or prior treatment with clozapine for treatment resistance; were pregnant or breastfeeding; had had a myocardial infarction in the previous 6 months; had a history of or a current QTc prolongation; had uncompensated congestive heart failure; had sustained cardiac arrhythmia, a first-degree heart block, or complete left bundle branch block; or had another serious and unstable medical condition.

A total of 1894 patients were screened for the study; 6.5% were excluded because they did not meet eligibility criteria, 5.8% refused, 1.7% decided they were not willing to change their antipsychotic medication, and 7.1% were not enrolled for other reasons.

The study enrolled a wide spectrum of patients with chronic and recurrent schizophrenia, ranging from partially remitted outpatients to exacerbated inpatients. With the specific exceptions previously noted, patients with medical or psychiatric comorbidity and those requiring concomitant medications were included. Overall, 58.4% of subjects had at least 1 co-occurring medical condition—disorders that would have excluded them from most clinical trials. The most common chronic medical conditions were as follows: hypertension (20.2% of the sample), hyperlipidemia (13.8%), and diabetes mellitus (10.7%). Substance abuse or dependence was identified in 35.7% of participants.

We report findings from 1-time baseline assessments¹⁹ conducted before randomization and before experimental treatments began. Baseline interviews were conducted with 1460 subjects at 56 CATIE sites. Data from 1 site (33 patients) were excluded from all analyses because of concerns about their quality.

MEASURES

The MacArthur Community Violence Interview²⁰⁻²² was used to measure violent behavior at 2 levels of severity during the past 6 months: minor violence, corresponding to simple assault without injury or weapon use; and serious violence, corresponding to any assault using a lethal weapon or resulting in injury, any threat with a lethal weapon in hand, or any sexual assault. A composite measure of any violence (minor or serious) was also analyzed.

For the measures of minor violence and any violence, self-report information was supplemented with family collateral re-

ports on parallel questions. A positive report from either the patient or the family collateral informant was treated as a positive indicator of any violence. Family collateral information regarding violent behavior was available for 617 participants at baseline.

Published reports from the MacArthur Violence Risk Assessment study, which developed the MacArthur Community Violence Interview, have labeled these 2 constructs as “violence” and “other aggressive acts.”²⁰ In this article, however, to be consistent with standard definitions of violent crime used in reports by the Bureau of Justice Statistics,²³ we use the common term *violence*, qualified by level of severity, to refer to these assaultive behaviors.

Independent variables were chosen for analysis based on prior clinical and epidemiological studies^{4,6,12,16,20,22} of risk factors related to violence and other outcomes for individuals with schizophrenia. We dichotomized covariates if warranted by their distribution or nonlinear association with violence.²⁴

Risk factors were measured by standardized and adapted interview questions from established instruments. Social contact and support were measured with items modified from the Duke Social Support Scale.²⁵ The Structured Clinical Interview for Axes I and II *DSM-IV* Disorders—Patient Edition¹⁸ was used to confirm diagnosis of schizophrenia and to assess childhood conduct problems. The Clinical Global Impression Scale was used to rate the severity of participants’ illness.²⁶ The Positive and Negative Syndrome Scale (PANSS)²⁷ is a clinical rating of individual psychotic symptoms on a 7-point scale from “symptom absent” to “extreme.” Two subscales from the PANSS were analyzed: positive psychotic symptoms (delusions, conceptual disorganization, hallucinations, excitement, grandiosity, suspiciousness/persecution, and hostility) and negative psychotic symptoms (blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, and stereotyped thinking). Depressive symptoms were assessed with the Calgary Depression Scale for Schizophrenia.²⁸ The Insight and Treatment Attitudes Questionnaire²⁹ was used to measure awareness of mental health problems and acknowledgment of need for treatment in the past, currently, and in the future. Substance use and abuse/dependence were assessed from multiple sources of information: hair and urine testing for illicit drug use, self-report, family report, clinician ratings on a screening inventory and the Alcohol or Drug Use Scale,³⁰ and Structured Clinical Interview for Axes I and II *DSM-IV* Disorders—Patient Edition diagnostic assessment.¹⁸ The Quality of Life Scale described by Heinrichs et al³¹ was used to measure functional performance in several areas: common objects and activities, instrumental role functioning, intrapsychic foundations, and interpersonal relations. The Instrumental Activities of Daily Living Scale assessed functioning in personal care and household chores.

Baseline assessments were conducted during a 1-time structured interview by trained clinical interviewers blind to random assignment for the subsequent follow-up study.^{4,19}

ANALYSIS

Multivariable models were estimated using mixed-model logistic regression³²⁻³⁴ with 3 dichotomous measures of violence: (1) minor violence vs no violence, (2) serious violence vs no serious violence, and (3) any violence vs no violence. Site was entered as a random effect.

For each violence outcome measure, bivariate associations with individual risk factors were first estimated. Separate multivariable models for each of the 5 domains were then estimated. Covariates were retained in the domain models at $P < .15$.

Finally, all covariates that were selected in the domain models were entered together into a final model, with selection at $P < .15$.

RESULTS

SAMPLE CHARACTERISTICS

Data including the violence measures were available for 1410 participants. The mean age of participants was 40.5 years. The sample was 74.3% male, 60.6% white, 34.8% African American, and 4.6% from other racial backgrounds. Only 19.2% were married or cohabiting. Of the sample, 25.4% had less than a high school education, 35.2% had completed high school, and 39.4% had attended college. Only 6.8% of participants were engaged in any substantial vocational activity. Of the participants, 27.4% had no health insurance and the remaining 72.6% had 1 or more of the following types of coverage: Medicaid (45.8%), Medicare (27.8%), Veterans Affairs (9.2%), and private insurance (9.1%).

During the past 30 days, 77.6% of participants lived independently in the community (eg, lived alone or with others in a private apartment or house), 13.8% lived in a minimally structured residence (eg, supervised apartment program or boarding home), 4.8% lived in a moderately restrictive residence (eg, halfway house, treatment program, or psychiatric diversion facility), 12.6% lived in extremely restrictive residences (eg, psychiatric hospital, skilled nursing facility, or jail), and 3.8% were homeless (eg, unsheltered or in an emergency homeless shelter). Some patients had lived in more than 1 of these types of settings.

Clinically, the sample was moderately symptomatic. The mean total PANSS score was 75 (possible range, 30-210), with a mean negative symptom score of 20 (possible range, 7-49) and a mean positive symptom score of 18 (possible range, 7-49). Average item-level scores on the PANSS were between 2 (minimal impairment) and 3 (mild impairment). The sample’s mean score on the Calgary Depression Scale for Schizophrenia was 4.6 (possible range, 0-27), with average item-level scores between 0 (absent) and 1 (mild). Of the participants, 35.7% had a substance abuse or dependence disorder; an additional 24.5% used alcohol or illicit drugs without significant impairment. Of the participants, 27.2% had a recent hospitalization or episode of crisis care. The mean time since first treatment with an antipsychotic medication was more than 16 years. Two thirds of participants reported a history of physical or sexual victimization before the age of 15 years, while about 1 in 5 participants reported some experience of victimization in the past 6 months.

To assess generalizability, we compared participants with a quasi-random sample of 1413 patients enrolled in the Schizophrenia Care and Assessment Program (SCAP), an observational noninterventive study of schizophrenia treatment in usual-care settings in the United States. The 2 samples were similar in demographic characteristics (eg, sex [69.6% male in SCAP and 74.4% male in CATIE]), age (mean age of 43 years in SCAP and 41 years in CATIE), and education (35.9% of SCAP participants had a high school education and 27.6%

attended college; in CATIE, these percentages were 35.2% and 39.4%, respectively). The CATIE project had a lower proportion of participants from racial minority backgrounds (39.8% vs 53.5%).

The samples also resembled each other in clinical characteristics. Nearly one third of the patients in both studies had recently been hospitalized. The CATIE sample had slightly higher average scores on psychotic symptom severity than the SCAP patients (mean PANSS total score, 75 vs 71), and had slightly higher scores on functioning and quality of life (mean Quality of Life Scale score, 63 vs 57) (Haya Ascher-Svanum, PhD, written communication, February 28, 2005). These similarities provide some confidence that the CATIE project's randomized controlled trial design did not result in a biased selection of more severely ill and impaired patients.

PREVALENCE OF VIOLENCE

Of the 1410 participants in the analysis, 1140 (80.9%) reported no violence, 219 (15.5%) reported minor violence only, and 51 (3.6%) reported serious violence. The 6-month prevalence of any violence was 19.1%. eTable 1 and eTable 2 (available at <http://www.archgenpsychiatry.com>) present prevalence of violence by sample characteristics.

CORRELATES OF MINOR VIOLENCE

Table 1 presents bivariate and adjusted odds ratios (ORs) for minor violence compared with no violence. The final model shows minor violent behavior was significantly more likely among participants with several non-clinical characteristics: younger age, female sex, limited or no vocational activity, residing in restrictive housing, residing with family or relatives, not feeling "listened to" by family members, and recent history of police contact. In the clinical/functional domain, minor violence was significantly associated with positive psychotic symptoms (higher PANSS positive scores), more years in treatment, co-occurring substance abuse/dependence, recent nonviolent victimization, and functional impairment in the area of leisure activities.

SEX EFFECT

Additional analyses revealed that the sex effect in the final model was influenced by a subgroup of younger women with substance abuse problems and history of arrest. Women in the sample were also more likely to live with family, thereby presumably having more opportunities for physical fights with social network members.³⁵

CORRELATES OF SERIOUS VIOLENCE

Table 2 presents parallel findings for serious violence. The final model shows that 3 covariates—younger age, childhood conduct problems, and arrest history—were significantly associated with serious violence. Among the clinical/functional variables, above-median PANSS positive scores increased serious violence risk, but above-median PANSS negative scores lowered risk.

Is the association of violence with positive schizophrenia symptoms conditioned on the relative absence of negative symptoms? To address this question, we tested the categorical interaction effect of positive and negative symptoms. Participants with a combination of above-median positive and below-median negative symptoms were at significantly elevated risk for serious violence (OR, 3.05; $P < .001$), compared with those with below-median scores on both types of symptoms. However, those with a combination of above-median positive and above-median negative symptoms were not more violent (OR, 0.95; $P = .90$); those with below-median positive and above-median negative symptoms were less violent (OR, 0.12; $P = .02$) (**Figure**).

In bivariate analysis, substance abuse/dependence was associated with a highly significant 4-fold increase in the odds of serious violent behavior. However, in the final model, covariates including psychotic symptoms and childhood conduct disorder rendered the effect of substance abuse nonsignificant. Thus, the effect of substance abuse on serious violence in this population may be indirect, mediated, or potentiated by psychopathological features and other factors.

CORRELATES OF ANY VIOLENCE

A final model for any violence resembled the model for minor violence with 1 exception: childhood conduct problems were significantly (OR, 1.50; $P = .02$) associated with any violence, but not with minor violence only (eTables 1 and 2; available at: <http://www.archgenpsychiatry.com>).

The analysis technique did not allow specific estimation of the proportion of variance explained by these models. However, a parallel analysis using conventional logistic regression, treating site as a class variable, suggests that the final models may account for approximately 18% of the variance in minor and serious violence. Significant site differences (which would incorporate urban population density and neighborhood characteristics) may explain an additional 7% of the variance in minor violence and an additional 16% of the variance in serious violence. These estimates must be interpreted with caution; they merely suggest that, even taking into account significant demographic, clinical, and site effects, most of the variability in violence in this population remains unexplained by these statistical models.

SPECIFIC PSYCHOTIC SYMPTOMS AND SERIOUS VIOLENCE

Additional item-level analyses were conducted to elucidate the association between serious violence and positive vs negative psychotic symptoms. Among the 7 symptom ratings that compose the PANSS positive subscale, 5 specific symptoms (hostility, suspiciousness/persecution, hallucinatory behavior, grandiosity, and excitement) were significantly associated with increased risk of serious violence. The rating of hostility assessed "verbal and nonverbal expressions of anger and resentment." For each unit increase on the 7-point rating of hostility, the odds of serious violence increased by a factor of 1.65 ($P < .001$).

Table 1. Risk Factors for Minor Violence

Model	OR (95% CI)		
	Bivariate Associations	Domain Models*	Final Model (N = 1115)
1: Demographic characteristics, social stratification, and housing			
Age	0.95 (0.94-0.96)†	0.95 (0.94-0.97)†	0.94 (0.92-0.96)†
Male sex	0.77 (0.56-1.05)	0.69 (0.49-0.97)‡	0.52 (0.35-0.78)§
Nonwhite race	1.13 (0.83-1.54)	NA	NA
Cohabitation	1.38 (0.98-1.94)	1.73 (1.20-2.51)§	NA
High monthly income	0.54 (0.40-0.73)†	0.77 (0.56-1.06)	NA
College education	0.78 (0.58-1.05)	NA	NA
Substantial vocational activity	0.20 (0.07-0.53)†	0.18 (0.06-0.49)†	0.17 (0.06-0.50)†
Housing during the past 30 d			
Extremely restrictive	3.04 (2.04-4.53)†	2.60 (1.72-3.92)†	1.70 (1.01-2.84)‡
Homeless	1.08 (0.52-2.23)	NA	NA
Low on economic scarcity	0.52 (0.35-0.76)†	0.55 (0.37-0.83)§	NA
2: Household composition and social contact			
Currently live			
Alone (reference)	NA	NA	NA
With family or other relatives	2.64 (1.79-3.90)†	3.45 (2.04-5.85)†	2.62 (1.47-4.67)†
With other people, not related	1.77 (1.13-2.80)§	2.28 (1.21-4.29)	1.61 (0.81-3.21)
Frequent contact with family and friends	1.29 (0.82-2.01)	NA	NA
Feel "listened to" most of the time by family	0.56 (0.41-0.77)†	0.59 (0.43-0.80)†	0.63 (0.44-0.91)§
3: Childhood risk factors			
Childhood physical abuse	1.52 (1.09-2.12)§	NA	NA
Childhood sexual abuse	1.82 (1.31-2.52)†	1.64 (1.18-2.28)§	NA
Childhood conduct problems (≥2)	1.90 (1.42-2.55)†	1.78 (1.32-2.39)†	NA
4: Current clinical characteristics, impairment, and functioning			
Clinical Global Impression Scale score	1.18 (1.01-1.37)‡	NA	NA
PANSS score			
Negative (above median)	1.06 (0.79-1.41)	NA	NA
Positive (above median)	1.81 (1.35-2.43)†	1.88 (1.36-2.60)†	1.66 (1.16-2.39)§
Calgary Depression Scale for Schizophrenia score	1.05 (1.02-1.08)§	NA	NA
Insight and Treatment Attitudes Questionnaire score (above median)	0.89 (0.66-1.19)	NA	NA
Years in treatment	0.97 (0.96-0.99)†	0.97 (0.96-0.99)†	1.03 (1.00-1.05)‡
Substance use			
Abstinent (reference)	NA	NA	NA
Use	1.54 (1.03-1.94)‡	1.39 (0.90-2.14)	1.41 (0.87-2.28)
Abuse or dependence	2.77 (1.96-3.93)†	2.29 (1.58-3.34)†	2.42 (1.59-3.69)
Recent victimization (past 6 mo)			
Violently victimized	3.53 (1.68-7.40)†	2.25 (0.92-5.53)	NA
Nonviolently victimized	2.04 (1.27-3.27)§	1.75 (1.00-3.05)‡	2.10 (1.12-3.94)
QOL Scale score			
Common objects and activities subscale	1.08 (0.88-1.34)	0.81 (0.70-0.93)§	NA
Instrumental role subscale	0.97 (0.83-1.12)	NA	NA
Intrapsychic foundations subscale	1.11 (0.90-1.37)	NA	NA
Interpersonal relations subscale	1.11 (0.92-1.34)	1.16 (1.01-1.33)‡	1.15 (0.98-1.34)
Leisure activities (past week)	0.61 (0.44-0.86)	0.71 (0.48-1.06)	0.56 (0.36-0.87)§
Instrumental ADLs (past week)	0.85 (0.28-2.54)	NA	NA
Satisfaction with life	0.86 (0.78-0.95)§	0.89 (0.80-0.99)‡	0.89 (0.70-1.00)‡
5: Institutional contact			
Total prior hospitalizations			
Lifetime, ≥4	0.96 (0.72-1.27)	0.76 (0.55-1.03)	NA
Past year, ≥2	2.16 (1.60-2.91)†	2.32 (1.68-3.19)†	1.35 (0.92-1.98)
Arrested or picked up for a crime (past 6 mo)	4.28 (2.67-6.84)†	4.11 (2.55-6.62)†	3.16 (1.76-5.69)

Abbreviations: ADL, activities of daily living; CI, confidence interval; NA, data not applicable; OR, odds ratio; PANSS, Positive and Negative Syndrome Scale; QOL, Quality of Life.

*N = 1346 for model 1, N = 1178 for model 2, N = 1355 for model 3, N = 1288 for model 4, and N = 1354 for model 5.

†P < .001.

‡P < .05.

§P < .01.

Suspiciousness and persecutory symptoms also showed a strong association with serious violence (OR, 1.46; P < .001). This symptom is characterized by "unrealistic or exaggerated ideas of persecution, as reflected in guard-

edness, a distrustful attitude, suspicious hypervigilance, or frank delusions that others mean one harm." The highest score was given when the patient manifested a "network of systematized persecutory delu-

Table 2. Risk Factors for Serious Violence

Model	OR (95% CI)		
	Bivariate Associations	Domain Models*	Final Model (N = 1401)
1: Demographic characteristics, social stratification, and housing			
Age	0.95 (0.93-0.98)†	0.95 (0.93-0.98)†	0.96 (0.94-0.99)‡
Male sex	1.32 (0.72-2.42)	NA	NA
Nonwhite race	1.37 (0.81-2.33)	NA	NA
Cohabitation	1.05 (0.56-1.97)	NA	NA
High monthly income	0.52 (0.30-0.89)§	NA	NA
College education	0.96 (0.58-1.60)	NA	NA
Substantial vocational activity	0.84 (0.29-2.40)	NA	NA
Housing during the past 30 d	NA	NA	NA
Extremely restrictive	1.85 (0.95-3.59)	NA	NA
Homeless	2.06 (0.79-5.35)	2.21 (0.83-5.89)	2.34 (0.80-6.82)
Low on economic scarcity	1.12 (0.52-2.42)	NA	NA
2: Household composition and social contact			
Currently live			
Alone (reference)	NA	NA	NA
With family or other relatives	1.21 (0.72-2.02)	NA	NA
With other people, not related	1.27 (0.72-2.24)	NA	NA
Frequent contact with family and friends	0.79 (0.41-1.53)	NA	NA
Feel "listened to" most of the time by family	0.75 (0.43-1.29)	NA	NA
3: Childhood risk factors			
Childhood physical abuse	2.28 (1.35-3.86)‡	NA	NA
Childhood sexual abuse	1.83 (1.06-3.16)§	NA	NA
Childhood conduct problems (≥2)	4.81 (2.69-8.62)†	4.81 (2.69-8.62)†	3.29 (1.79-6.07)†
4: Current clinical characteristics, impairment, and functioning			
Clinical Global Impression Scale score	1.22 (0.93-1.60)	NA	NA
PANSS score			
Negative (above median)	0.31 (0.17-0.56)†	0.26 (0.14-0.49)†	0.25 (0.13-0.47)†
Positive (above median)	3.00 (1.69-5.31)†	2.94 (1.63-5.30)†	2.71 (1.46-5.06)‡
Calgary Depression Scale for Schizophrenia score	1.09 (1.04-1.15)†	1.07 (1.01-1.13)§	1.08 (1.02-1.14)‡
Insight and Treatment Attitudes Questionnaire score (above median)	1.16 (0.70-1.91)	NA	NA
Years in treatment	0.98 (0.95-1.00)	0.97 (0.95-1.00)	NA
Substance use			
Abstinent (reference)	NA	NA	NA
Use	2.46 (1.09-5.60)§	2.42 (1.07-5.48)§	1.88 (0.78-4.51)
Abuse or dependence	4.11 (1.99-8.52)†	3.38 (1.61-7.10)†	2.10 (0.94-4.71)
Recent victimization (past 6 mo)			
Violently victimized	4.88 (1.99-11.93)†	2.57 (0.96-6.92)‡	NA
Nonviolently victimized	3.84 (2.08-7.09)†	2.87 (1.48-5.55)†	2.27 (1.12-4.61)§
QOL Scale score			
Common objects and activities subscale	1.08 (0.88-1.34)	NA	NA
Instrumental role subscale	0.97 (0.83-1.12)	NA	NA
Intrapsychic foundations subscale	1.11 (0.90-1.37)	NA	NA
Interpersonal relations subscale	1.11 (0.92-1.34)	NA	NA
Leisure activities (past week)	1.19 (0.60-2.36)	NA	NA
Instrumental ADLs (past week)	NA	NA	NA
General life satisfaction	0.83 (0.46-1.51)	NA	NA
5: Institutional contact			
Total prior hospitalizations			
Lifetime, ≥4	0.93 (0.57-1.53)	NA	NA
Past year, ≥2	1.44 (0.86-2.40)	NA	NA
Arrested or picked up for crime (past 6 mo)	5.85 (3.18-10.76)†	5.85 (3.18-10.76)†	3.45 (1.74-6.85)†

Abbreviations: See Table 1.

*N = 1405 for model 1, N = 1406 for model 3, N = 1348 for model 4, and N = 1407 for model 5.

†P < .001.

‡P < .01.

§P < .05.

sions [which] dominates the patient's thinking, social relations, and behavior."

Serious violence was also strongly associated with hallucinatory behavior (OR, 1.43; P < .001). This

symptom is characterized by auditory, visual, or other perceptions that are not generated by external stimuli; the highest score was assigned when the patient reported these false perceptions and gave the percep-

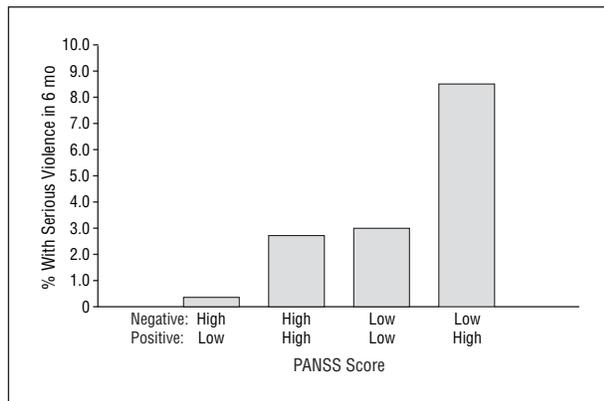


Figure. Serious violent behavior and Positive and Negative Syndrome Scale (PANSS) scores. Violent behavior is defined as behavior that causes bodily injury or the use of a lethal weapon to harm another person.

tions “a rigid delusional interpretation,” and when the perceptions “provoke[d] verbal and behavior responses, including obedience to command hallucinations.”

Finally, serious violence was significantly associated with grandiosity (OR, 1.31; $P < .001$), characterized as “exaggerated self-opinion and unrealistic conviction of superiority, including delusion of extraordinary abilities,” and excitement symptoms (OR, 1.30; $P = .02$), characterized as “hyperactivity as reflected in accelerated motor behavior, heightened responsivity to stimuli, hypervigilance, or excessive mood lability.”

Two other PANSS-positive symptoms were not, by themselves, associated with serious violence: conceptual disorganization, characterized by incoherent thinking, and a general rating of delusions, denoting “beliefs which are unfounded, and idiosyncratic.” However, an interaction analysis showed that the combination of delusional thinking with suspiciousness/persecutory ideation was highly associated with serious violence: patients scoring above the median on the general delusions scale and the suspiciousness/persecution scale were 2.9 times ($P < .001$) more likely to be seriously violent than those scoring below the median on both of these symptom ratings. Patients with above-median scores on general delusions combined with below-median scores on suspiciousness/persecution did not display a higher risk of serious violence (OR, 0.77; $P = .63$). In contrast, participants with above-median scores on suspiciousness/persecution and below-median scores on general delusions were significantly more likely to be seriously violent (OR, 2.6; $P = .02$). However, this last symptom combination was rare. Because high suspiciousness and high delusions were highly correlated ($\chi^2 = 248$, $P < .001$), the combination of high suspiciousness with low delusions affected a relatively small subgroup (174 patients [12.3% of the total sample]), of which 9 patients reported serious violent behavior.

Among the 7 symptoms that compose the PANSS negative subscale, 5 specific symptom ratings were significantly associated with decreased risk of serious violence: lack of spontaneity and flow of conversation (OR, 0.66; $P < .001$), passive/apathetic social withdrawal (OR, 0.67; $P < .001$), blunted affect (OR, 0.75; $P < .001$), poor

rapport (OR, 0.79; $P = .03$), and difficulty in abstract thinking (OR, 0.84; $P < .001$).

COMMENT

We find that the 6-month prevalence of any violent behavior in this sample of schizophrenia patients selected for a randomized clinical trial was 19.1%. This is slightly higher than the 15.3% 6-month prevalence rate reported in a recent observational study of schizophrenia patients sampled from usual-care settings.²² We find that distinct, but overlapping, profiles of risk are linked to minor vs serious violent behavior in persons with schizophrenia. Violence in this population is associated with multiple factors,³⁶ with an important role attributable to psychotic symptoms; premorbid developmental events,³⁷⁻⁴⁰ such as childhood conduct problems; and current social situation, such as increased opportunity for violence presented by living with family members.

Minor and serious violence were significantly more prevalent in CATIE participants with a higher level of positive psychotic symptoms. Does this conflict with or advance knowledge from previous studies? The landmark MacArthur Violence Risk Assessment Study⁹ found that the presence of psychotic delusions did not increase the prospective risk of violent behavior in a diagnostically heterogeneous sample of psychiatric patients (17% with schizophrenia) who were recently discharged from hospitals. However, Appelbaum and colleagues^{9(p531)} suggested a theoretically compelling reason for their negative findings: “[D]elusions are often associated with chronic psychotic conditions that are frequently attended by social withdrawal and the development of smaller social networks. Delusional subjects in the community, therefore, may have less desire and fewer opportunities to engage in the interpersonal interactions that can lead to violence compared with less severely ill patients.” The MacArthur study investigators were not able to test this hypothesis with their data, but suggested it would be an important avenue for future research.

The CATIE baseline findings on violence, taken as a whole, provide new evidence that is consistent with the hypothesis of Appelbaum et al.⁹ Specifically, we found that patients living alone were significantly less likely to engage in any violence than their counterparts who were living with family, controlling for other risk factors. Our analysis also showed that high negative psychotic symptoms were significantly associated with reduced risk of serious violence, and that they moderated the effect of the positive symptoms; violence was significantly increased by positive symptoms, but only when negative symptoms were low. This finding has intuitive clinical plausibility. A certain level of initiative, organization, psychomotor activation, and social contact may be necessary to carry out violent acts; those conditions tend to be absent in persons with high negative symptoms of schizophrenia.

Nonclinical variables, such as family coresidence, may affect violence risk in complex ways, either preventing or provoking violent behavior, depending on whether the family environment serves as a protective matrix or an opportunity for aggressive interactions. Consistent with

some previous reports,^{41,42} our study presents a complex picture of the linkage between violence, social contact, and social support. Respondents living with family were more likely to report engaging in any violent behavior. Female participants, in particular, were more likely than male participants to live with family, thereby presumably having more opportunities for physical fights with social network members,³⁵ and, indeed, females in this sample were significantly more likely to engage in minor violence than their male counterparts, controlling for other significant variables. A subgroup of younger women with substance abuse problems largely accounted for this (unusual) finding, and there was no sex association with serious violence.

This pattern in the data could have been due to a treatment selection effect; where men were more likely in general to be treated for schizophrenia (accounting for nearly three quarters of the sample), it is possible that some women with schizophrenia may not have been identified by the service system until, or unless, they engaged in socially problematic behavior, such as minor violence. Moreover, as mentioned, because women with this disease are more likely to be living with family, it may be that family members who become targets of assaultive behavior are instrumental in bringing their mentally ill relative into treatment.

At the same time, family relationships that apparently provided a supportive audience were protective. We found that subjects who felt "listened to . . . most of the time" by their family members were only about half as likely to behave violently as subjects who did not report feeling listened to by family.

Our findings regarding substance abuse also warrant comment. The significant bivariate effect of substance abuse on serious violence was rendered nonsignificant in the final model when controlling for age, PANSS positive symptoms, childhood conduct problems, and recent victimization. This suggests that the effect of substance abuse on serious violence may be mediated by these other covariates.

This study is limited in several ways. First, these cross-sectional data cannot demonstrate causal connections between variables; rather, they show statistical associations, which may be consistent with a given causal formulation. Second, the study relied heavily on self-report for its key measure of violence, which may have underestimated the true incidence of these socially undesirable behaviors. (Collateral information from family members regarding subjects' recent violent behavior was available for 617 of the 1410 subjects.) However, self-report remains the best method available for distinguishing between minor violence and serious violence, one of the main objectives of this article. Specifically, collateral informants often do not possess detailed information regarding violent acts in persons with schizophrenia, and because most violent behavior never results in arrest, criminal records are also inadequate to detect violence or differentiate between minor and serious violence. The third limitation is that participants in the CATIE project may not be representative of all persons with schizophrenia. The CATIE sample is a diverse group of treated schizophrenia patients who were willing to en-

roll in a medication trial. The study excluded first-episode patients (who might have been less violent) and wholly treatment-refractory patients (who might have been more violent) and, thus, the findings cannot generalize to such patients. However, only 7% of screened patients were excluded for this (or any other) eligibility criterion, and the study population resembled a usual-care, quasi-random, observational, noninterventional study sample (SCAP) in its demographic and clinical characteristics.

In conclusion, serious violent behavior, although generally uncommon in people with mental disorder,³⁶ carries a high human and social cost,⁴³⁻⁴⁶ which is reflected in psychiatrists' concerns about their own legal liability whenever they make treatment decisions involving patients who may be assaultive. The likelihood that some individuals with schizophrenia may commit assaultive acts is a significant risk to be addressed by providers and caregivers, and is a significant limitation in the move to normalize mental health services within the community. More informed and nuanced explanatory models, particularly in the clinical domain, are needed to improve understanding of how and why violent behavior occurs in persons with schizophrenia with particular characteristics, under varying conditions of social life.

To the extent that violence risk is significantly increased by positive psychotic symptoms, the crucial role of symptom management becomes clear (eg, through effective pharmacotherapy and patient adherence). However, to the extent that risk of violence (particularly minor violence) is increased by other, nonclinical, variables, such as female sex, household composition, social interaction, and lack of vocational or leisure activity, the clinical lesson is that violence risk management must include a focus on the whole person in the community environment.

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Additional Resources: The online-only eTables are available at <http://www.genpsychiatry.com>.

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Table 1. Prevalence of Violence During the Past 6 Months by Sample Characteristics

Variable	Total No. (N = 1410)	Minor Violence (n = 219)*†	Serious Violence (n = 51)*†	Any Violence (n = 270)*
Demographic characteristics, social stratification, and housing				
Age				
Below median (<42 y)	681	149 (21.88)	32 (4.70)	181 (26.58)
Median or above (≥42 y)	729	70 (9.60)	19 (2.61)	89 (12.21)
Sex				
Female	362	65 (17.96)	11 (3.04)	76 (20.99)
Male	1048	154 (14.69)	40 (3.82)	194 (18.51)
Race				
White	849	125 (14.72)	26 (3.06)	151 (17.79)
Nonwhite	561	94 (16.76)	25 (4.46)	119 (21.21)
Marital status				
Single	1140	167 (14.65)	41 (3.60)	208 (18.25)
Married, cohabitating	270	52 (19.26)	10 (3.70)	62 (22.96)
Income				
Below median	701	141 (20.11)	34 (4.85)	175 (24.96)
Median or above	702	78 (11.11)	17 (2.42)	95 (13.53)
Education				
High school or less	854	143 (16.74)	31 (3.63)	174 (20.37)
College	556	76 (13.67)	20 (3.60)	96 (17.27)
Substantial vocational activity				
No	1308	213 (16.28)	48 (3.67)	261 (19.95)
Yes	97	4 (4.12)	3 (3.09)	7 (7.22)
Extremely restrictive housing (past 30 d)				
No	1231	167 (13.57)	41 (3.33)	208 (16.90)
Yes	177	52 (29.38)	10 (5.65)	62 (35.03)
Homeless				
No	1354	209 (15.44)	47 (3.47)	256 (18.91)
Yes	53	9 (16.98)	4 (7.55)	13 (24.53)
Enough money for necessities				
No	175	44 (25.14)	6 (3.43)	50 (28.57)
Yes	1233	175 (14.19)	45 (3.65)	220 (17.84)
Household composition and social contact				
Currently live				
Alone	346	25 (7.23)	8 (2.31)	33 (9.54)
With family	768	152 (19.79)	30 (3.91)	182 (23.70)
With others, not related	296	42 (14.19)	13 (4.39)	55 (18.58)
Frequent contact with family and friends				
No	210	24 (11.43)	9 (4.29)	33 (15.71)
Yes	1199	195 (16.26)	42 (3.50)	237 (19.77)
Feel "listened to" most of the time by family				
No	603	115 (19.07)	23 (3.81)	138 (22.89)
Yes	616	77 (12.50)	18 (2.92)	95 (15.42)
Childhood history				
Physical abuse				
No	1130	162 (14.34)	32 (2.83)	194 (17.17)
Yes	278	57 (20.50)	19 (6.83)	76 (27.34)
Sexual abuse				
No	1122	155 (13.81)	34 (3.03)	189 (16.84)
Yes	284	64 (22.54)	17 (5.99)	81 (28.52)
Conduct problems				
No	934	121 (12.96)	15 (1.61)	136 (14.56)
Yes	475	98 (20.63)	36 (7.58)	134 (28.21)
Current clinical characteristics, impairment, and functioning				
Clinical Global Impression Scale score				
Normal to mildly ill	390	55 (14.10)	9 (2.31)	64 (16.41)
Moderately to very severely ill	1014	162 (15.98)	42 (4.14)	204 (20.12)
PANSS score				
Negative				
Below median	753	112 (14.87)	40 (5.31)	152 (20.19)
Median or above	655	106 (16.18)	11 (1.68)	117 (17.86)
Positive				
Below median	720	87 (12.08)	14 (1.94)	101 (14.03)
Median or above	688	131 (19.04)	37 (5.38)	168 (24.42)

(continued)

Table 1. Prevalence of Violence During the Past 6 Months by Sample Characteristics (cont)

Variable	Total No. (N = 1410)	Minor Violence (n = 219)*†	Serious Violence (n = 51)*†	Any Violence (n = 270)*
Current clinical characteristics, impairment, and functioning (cont)				
Calgary Depression Scale for Schizophrenia score				
Below median	936	134 (14.32)	20 (2.14)	154 (16.45)
Median or above	472	85 (18.01)	30 (6.36)	115 (24.36)
Insight and Treatment Attitudes Questionnaire score				
Below median	768	127 (16.54)	27 (3.52)	154 (20.05)
Median or above	640	91 (14.22)	24 (3.75)	115 (17.97)
Time in treatment				
Below median (<15 y)	717	113 (15.76)	26 (3.63)	139 (19.39)
Median or above (≥15 y)	637	100 (15.70)	25 (3.92)	125 (19.62)
Substance use				
Abstinent	562	55 (9.79)	8 (1.42)	63 (11.21)
Use	345	49 (14.20)	13 (3.77)	62 (17.97)
Abuse or dependence	503	115 (22.86)	30 (5.96)	145 (28.83)
Violently victimized (past 6 mo)				
No	1375	207 (15.05)	46 (3.35)	253 (18.40)
Yes	34	12 (35.29)	5 (14.71)	17 (50.00)
Nonviolently victimized (past 6 mo)				
No	1301	193 (14.83)	39 (3.00)	232 (17.83)
Yes	107	26 (24.30)	12 (11.21)	38 (35.51)
QOL Scale score				
Common objects and activities subscale				
Below median	648	120 (18.52)	23 (3.55)	143 (22.07)
Median or above	758	99 (13.06)	28 (3.69)	127 (16.75)
Instrumental role subscale				
Below median	728	122 (16.76)	28 (3.85)	150 (20.60)
Median or above	674	95 (14.09)	23 (3.41)	118 (17.51)
Intrapsychic foundations subscale				
Below median	644	117 (18.17)	19 (2.95)	136 (21.12)
Median or above	760	101 (13.29)	32 (4.21)	133 (17.50)
Interpersonal relations subscale				
Below median	681	111 (16.30)	16 (2.35)	127 (18.65)
Median or above	725	107 (14.76)	35 (4.83)	142 (19.59)
Leisure activities (past week)				
No	255	53 (20.78)	8 (3.14)	61 (23.92)
Yes	1153	166 (14.40)	43 (3.73)	209 (18.13)
Instrumental ADL (past week)				
No	19	4 (21.05)	0	4 (21.05)
Yes	1390	215 (15.47)	51 (3.67)	266 (19.14)
How do you feel about your life in general?				
Delighted to mixed	1081	152 (14.06)	40 (3.70)	192 (17.76)
Mostly dissatisfied to terrible	321	67 (20.87)	11 (3.43)	78 (24.30)
Service use, institutional contact, and treatment engagement				
Total hospitalizations				
Lifetime				
Below median (<4)	709	114 (16.08)	27 (3.81)	141 (19.89)
Median or above (≥4)	698	105 (15.04)	24 (3.44)	129 (18.48)
Past year				
Below median (<2)	839	95 (11.32)	26 (3.10)	121 (14.42)
Median or above (≥2)	568	124 (21.83)	25 (4.40)	149 (26.23)
Arrested or picked up for a crime (past 6 mo)				
No	1316	184 (13.98)	37 (2.81)	221 (16.79)
Yes	93	35 (37.63)	14 (15.05)	49 (52.69)

Abbreviations: ADL, activities of daily living; PANSS, Positive and Negative Syndrome Scale; QOL, Quality of Life.

*Data are given as number (percentage) of the sample. Percentages are based on row totals. Of the total sample, minor violence occurred in 15.53%; serious violence, 3.62%; and any violence, 19.15%.

†For serious violence, 3 persons had missing information. Percentages for minor violence and serious violence may not sum to the total percentage for any violence due to rounding.

eTable 2. Risk Factors for Any Violence

Model	Bivariate Associations		Domain Models*		Final Model (N = 1161)	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
1: Demographic characteristics, social stratification, and housing						
Age	0.95 (0.94-0.96)	<.001	0.95 (0.94-0.96)	<.001	0.94 (0.92-0.96)	<.001
Male sex	0.86 (0.64-1.16)	NA	0.75 (0.55-1.04)	NA	0.51 (0.35-0.74)	<.001
Nonwhite race	1.13 (0.85-1.51)	NA	NA	NA	NA	NA
Cohabitation	1.31 (0.95-1.80)	NA	1.66 (1.18-2.34)	<.01	NA	NA
High income	0.53 (0.40-0.70)	<.001	0.76 (0.56-1.02)	NA	NA	NA
College education	0.79 (0.60-1.04)	NA	NA	NA	NA	NA
Substantial vocational activity	0.29 (0.14-0.62)	<.01	0.26 (0.12-0.57)	<.001	0.21 (0.09-0.51)	<.001
Housing during the past 30 d						
Extremely restrictive	2.96 (2.03-4.32)	<.001	2.50 (1.70-3.68)	<.001	1.93 (1.23-3.03)	<.01
Homeless	1.25 (0.66-2.38)	NA	NA	NA	NA	NA
Low on economic scarcity	0.57 (0.40-0.83)	<.01	0.62 (0.42-0.91)	<.01	NA	NA
2: Household composition and social contact						
Currently live						
Alone (reference)	NA	NA	NA	NA	NA	NA
With family or other relatives	2.41 (1.69-3.45)	<.001	3.25 (2.00-5.27)	<.001	2.64 (1.56-4.47)	<.001
With other people, not related	1.77 (1.17-2.68)	<.01	2.35 (1.32-4.19)	<.01	1.55 (0.83-2.89)	NA
Frequent contact with family and friends	1.13 (0.76-1.67)	NA	NA	NA	NA	NA
Feel "listened to" most of the time by family	0.59 (0.44-0.78)	<.001	0.61 (0.45-0.82)	<.001	0.61 (0.44-0.85)	<.01
3: Childhood risk factors						
Physical abuse	1.67 (1.23-2.26)	<.001	1.27 (0.92-1.75)	NA	NA	NA
Sexual abuse	1.84 (1.36-2.48)	<.001	1.54 (1.13-2.11)	<.01	NA	NA
Conduct problems (≥2)	2.30 (1.75-3.01)	<.001	2.05 (1.55-2.71)	<.001	1.50 (1.06-2.11)	<.05
4: Current clinical characteristics, impairment, and functioning						
Clinical Global Impression Scale score	1.19 (1.03-1.38)	<.05	NA	NA	NA	NA
PANSS score (above median)						
Negative	0.87 (0.67-1.15)	NA	0.75 (0.55-1.03)	NA	0.72 (0.51-1.02)	NA
Positive	2.02 (1.53-2.67)	<.001	2.08 (1.53-2.84)	<.001	1.86 (1.32-2.62)	<.001
Calgary Depression Scale for Schizophrenia score	1.06 (1.03-1.09)	<.001	1.04 (1.00-1.07)	<.05	NA	NA
Insight and Treatment Attitudes Questionnaire score (above median)	0.94 (0.72-1.23)	NA	NA	NA	NA	NA
Time in treatment (years)	0.97 (0.96-0.99)	<.001	0.97 (0.96-0.99)	<.001	1.02 (1.00-1.05)	<.05
Substance use						
Abstinent (reference)	NA	NA	NA	NA	NA	NA
Use	1.60 (1.10-1.98)	<.01	1.50 (1.00-2.24)	<.05	1.35 (0.86-2.12)	NA
Abuse or dependence	3.01 (2.17-4.18)	<.001	2.42 (1.70-3.45)	<.001	2.28 (1.53-3.41)	<.001
Recent victimization (past 6 mo)						
Violently victimized	4.00 (2.03-7.89)	<.001	2.19 (0.99-4.82)	NA	NA	NA
Nonviolently victimized	2.43 (1.60-3.69)	<.001	2.19 (1.34-3.58)	<.01	2.36 (1.34-4.15)	<.01
QOL Scale score						
Common objects and activities subscale	0.81 (0.73-0.91)	<.001	0.83 (0.72-0.95)	<.01	NA	NA
Instrumental role subscale	0.94 (0.87-1.03)	NA	NA	NA	NA	NA
Intrapsychic foundations subscale	0.89 (0.79-0.99)	<.05	NA	NA	NA	NA
Interpersonal relations subscale	1.00 (0.91-1.11)	NA	1.16 (1.02-1.32)	<.05	1.13 (0.98-1.30)	NA
Leisure activities (past week)	0.67 (0.48-0.92)	<.01	0.73 (0.50-1.07)	NA	0.57 (0.37-0.87)	<.01
Instrumental ADL (past week)	1.13 (0.38-3.38)	NA	NA	NA	NA	NA
General life satisfaction	0.87 (0.80-0.96)	<.01	NA	NA	NA	NA
5: Institutional contact						
Total prior hospitalizations						
Lifetime, ≥4	0.95 (0.73-1.23)	NA	0.76 (0.57-1.02)	NA	NA	NA
Past year, ≥2	2.02 (1.53-2.67)	<.001	2.16 (1.61-2.91)	<.001	NA	NA
Arrested or picked up for a crime (past 6 mo)	4.93 (3.20-7.60)	<.001	4.69 (3.03-7.27)	<.001	3.26 (1.91-5.56)	<.001

Abbreviations: ADL, activities of daily living; CI, confidence interval; NA, data not applicable; OR, odds ratio; PANSS, Positive and Negative Syndrome Scale; QOL, Quality of Life.

*N = 1397 for model 1, N = 1219 for model 2, N = 1406 for model 3, N = 1344 for model 4, and N = 1405 for model 5.