Reducing Violence Risk in Persons With Schizophrenia: Olanzapine Versus Risperidone

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Objective: This study prospectively examined the effectiveness of treatment with olanzapine versus risperidone in reducing violent behavior among patients with schizophrenia under "usual care" conditions in the community.

Method: Participants were 124 adults with DSM-IV–diagnosed schizophrenia-spectrum disorders receiving services in public-sector mental health systems in North Carolina. After enrollment (1997–1999), subjects were followed for 3 years in an observational study with interviews at 6-month intervals to assess treatment, clinical outcomes, and violent behavior. Rates of violence were compared over time between periods of first switch to olanzapine or risperidone and periods following at least 1 year of treatment with each of these medications.

Results: The study found that remaining on olanzapine for 1 year or more significantly lowered violence risk compared to first switch period, but no significant change in violence risk was found for subjects remaining on risperidone for 1 year or more. These results were obtained using multivariable time-series analysis controlling for salient demographic and clinical covariates.

Conclusion: This study found that, in the complex "real world" settings where persons with schizophrenia reside, long-term treatment with olanzapine confers some advantage over risperidone in reducing violence risk. This advantage appears to be at least in part an indirect effect, via improvement in adherence with treatment. Specifically, adherence with prescribed medication was found to mediate the association between olanzapine treatment and reduced violent behavior.

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Although violent behavior in the community is generally uncommon among persons with schizophrenia, an increased risk for violence has been found in subgroups of patients with co-occurring substance abuse problems who are nonadherent with prescribed psychiatric treatment and those with a history of frequent relapses resulting in hospitalization or arrest.[1–14] The potential for violence in these subgroups of patients increases public fear, prevents acceptance and inclusion of persons with psychiatric disabilities in society, disrupts continuity of care, and limits the effectiveness of community-based mental health services.[15–19]

As clinicians have become more aware of their potential liability for inadequate assessment and management of these patients,[20] clinical concerns about violence risk have increased.[21–25] One clinical strategy with promising implications for improved management of violence risk in schizophrenia treatment has been the use of "atypical" antipsychotic medications—including clozapine, risperidone, olanzapine, quetiapine, and ziprasidone.[26,27] Evidence from controlled trials of atypical antipsychotic agents indicates that these medications represent a significant improvement over conventional neuroleptics, with equal or improved efficacy in controlling positive and negative symptoms of schizophrenia, coupled with reduced adverse extrapyramidal symptoms.[28–31] A growing body of clinical research has also suggested that the atypical antipsychotic medications might be more efficacious in reducing aggressive and violent behavior in some patients with schizophrenia.[32–35]

Earlier research focused on demonstrating the efficacy of clozapine in reducing aggression.[35–41] These studies generally corroborated anecdotal clinical reports that patients with schizophrenia who take clozapine are less likely to engage in physical and verbal aggression.[37] The most recent research has examined the effects of risperidone and olanzapine on aggression in schizophrenia as well as other neuropsychiatric disorders.[42] Studies have shown that among patients with schizophrenia, risperidone treatment is associated with reduced Positive and Negative Syndrome Scale hostility scores,[43] Brief Psychiatric Rating Scale hostility scores,[29] and inpatient violent behavior.[44] Olanzapine has also been shown to reduce hostility in patients with schizophrenia[35] and to reduce violent behavior among individuals with

Alzheimer's disease,[45] Huntington's disease,[46] and developmental disabilities.[47,48]

Although atypical antipsychotics in general appear to reduce violence in schizophrenia, little is known about whether this effect is equivalent across these medications. One study has compared atypical antipsychotics on ratings of hostility among inpatients,[35] but to our knowledge there has been no examination of the effect of different atypicals on community violence among outpatients with schizophrenia. In particular, while olanzapine and risperidone have been shown to ameliorate hostility in schizophrenia, the 2 medications have distinct psychopharmacologic profiles,[49,50] influence cognitive functioning differently,[51–53] and have shown dissimilar levels of patient adherence.[54,55] However, biochemical,[56] neurocognitive,[57] and social-behavioral[9,58] factors can each substantially influence violence potential in schizophrenia. As a result, risperidone and olanzapine may have differential effects on violence among patients with schizophrenia—especially in community settings where nonadherence and substance abuse can further enhance risk. The purpose of this study is to explore and compare effects on reduced violent behavior in the community attributable to treatment with 1 of 2 of the most commonly prescribed atypical antipsychotic medications—olanzapine versus risperidone—using data from a naturalistic study of schizophrenia treatment, carried out under "usual care" conditions in a public mental health services system.

METHOD

Study Design and Sample

The data used for this analysis are from the North Carolina site of the Schizophrenia Care and Assessment Program (SCAP), a multicenter, prospective, observational study focused on assessing the clinical, functional, and service utilization outcomes associated with routine care, both pharmacologic and nonpharmacologic, for persons diagnosed with schizophrenia in 5 geographic regions of the United States. In North Carolina, a sample of 403 persons with schizophrenia-related disorders was recruited from several treatment facilities in an "open" system of care across a 9-county, mixed urban and rural area in the north-central region of the state. These individuals were enrolled using 2 recruitment strategies simultaneously, with screening for inclusion diagnoses: (1) sequential inpatient admissions at a regional public psychiatric hospital, an acute psychiatric unit of a private university hospital, and a veterans hospital; and (2) random selection of outpatients from 4 area mental health programs' case rosters and 1 veterans medical center outpatient clinic. Enrollment began in 1997 and was complete in 1999. Subjects in this recently completed study were followed for 3 years with clinical data collection at 6-month intervals. Methods included (1) structured interviews conducted in person, (2) review and abstraction of medical records, (3) electronic retrieval of data from health care management information systems on services utilization and costs, and (4) retrieval of arrest records from the North Carolina Department of Justice archival database. The SCAP research design is naturalistic and observational, with the purpose of understanding routine clinical care practices and treatment outcomes, and, therefore, conducted no experimental intervention or interference with usual patterns of treatment.

Diagnoses were based on review of clinical records. Since the SCAP was designed as an observational study of the treatment of persons *diagnosed with* schizophrenia under usual care conditions, all adult patients in treatment with recently documented DSM-IV diagnoses of schizophrenia, schizoaffective disorder, or schizophreniform disorder were eligible for the study. Because the aim of the study was to examine the treatment of patients who were diagnosed as having schizophrenia, chart diagnoses assigned in the past year were accepted prima facie and not verified by additional research diagnostic assessments upon enrollment. Participants also had to be able and willing to provide informed consent, had to be 18 years of age or older, and must not have participated in a clinical drug trial within 30 days prior to enrollment. Institutional review board approval was obtained at participating study sites prior to the initiation of the study, and informed consent was received from all participants. Analyses for this report involved a subsample of 124 individual patients treated primarily with olanzapine or risperidone, for a total of 357 person-period observations (i.e., the product of the number of individual subjects times the number of available 6-month observational periods for each subject) over a total of 3 years.

Measures

Violent behavior was measured with a composite index that combined 3 sources of data: (1) subject self-report using the MacArthur Community Violence Interview (MCVI)[59]; (2) systematic review of outpatient and inpatient medical records, including civil commitment documents and other legal information, using a chart-abstraction instrument for coding evidence of violence that was developed in the Duke Mental Health Study[60]; and (3) review of records of arrests for violent offenses documented in the North Carolina Department of Justice database. *Violent behavior* was defined operationally as any assault or battery committed against another person involving physical contact intended to harm (e.g., hitting, shoving, kicking, biting) or threatening another person with a lethal weapon in hand. Assaultive behavior meeting this definition that was reported from any 1 of the 3 sources was considered a positive indicator of violence.

Type of pharmacologic treatment was coded into 2 mutually exclusive categories for each 6-month period of

observation, using data collected from medical record abstractions: (1) any prescription for olanzapine remaining in effect for more than half the given period and (2) any prescription for risperidone remaining in effect for more than half the given period.

We did not have sufficient data to allow an informative analysis of the causes or effects of dosing differences, polypharmacy and the potential contribution of adjunct medications (such as β-blockers, anticonvulsants, or benzodiazepines), and any potential differences by route of administration of conventional neuroleptics, i.e., depot versus oral medications.

For the purpose of causal modeling that assumes temporal ordering in longitudinal time-series analysis, treatment effects were lagged, with models estimating associations between treatment with olanzapine or risperidone in a given 6-month period and violent behavior in the subsequent 6-month period. Had we not lagged the treatment period, we would not have been able to tell the direction of causality in any association between medication type and violence, i.e., whether the medication had caused a reduction in violence or, rather, whether violence had precipitated a change to a new type of medication. Finally, if over the course of the study, patients' prescriptions for either olanzapine or risperidone were discontinued, subsequent follow-up observations for these patients are not included in these analyses.

To control for possible selection effects, we classified observations into 2 groups within each drug treatment category: (1) drug switching periods, i.e., the first 6 months of follow-up after the period of initial switch to the new medication and (2) all subsequent periods with prescriptions remaining in effect for most of each period. To ensure correct classification of new drug initiation periods, the outcome analysis is prospective and begins with the second wave of treatment data predicting the third wave of violence data (i.e., using the first wave to eliminate patients who had already been taking olanzapine or risperidone for at least 6 months when the study began).

Medication compliance was measured at each 6-month assessment using a self-report item with a 5-point fixed response scale, coded 1 (I never missed taking my medicine) to 5 (I stopped taking the medicine altogether).

Mental health services utilization intensity was coded as a simple count of the number of outpatient service encounters during the 6-month period. This included visits for outpatient therapy, case management, medication checks, and any other billable encounter with a mental health service provider.

Demographic covariates included age, gender, and race (African American vs. white/other). Baseline clinical predictors that were examined included recent psychiatric hospitalization history (0 vs. 1 or more admissions in the past year), Global Assessment of Functioning (GAF) score,[61] and co-occurring substance use, assessed using clinician ratings on the Alcohol Use Scale (AUS)[62] and the Drug Use Scale (DUS).[62] Psychotic symptoms and adverse medication side effects were measured using the SCAP health questionnaire.[63] Psychotic symptoms were assessed using a 5-item scale, and adverse medication side effects were assessed using a 4-item scale. Responses for each of the 2 scales ranged from 1 (not at all) to 5 (extremely). Each subject's mean score for the respective scale was calculated; subjects scoring above the median on these scales were considered to have high psychotic symptoms and adverse medication side effects.

These independent variables were chosen for analysis based on prior clinical and epidemiological studies of risk factors related to violence and in order to control variability in violence risk that may be associated with severity of psychopathology, substance abuse comorbidity, prior hospital recidivism, and sociodemographic characteristics. Since this was an observational study without random assignment to treatment regimen, and since treatment selection may covary naturalistically with clinical as well as demographic risk factors for violence, it was necessary to control for putative predictors of both violence and treatment in order to properly interpret longitudinal treatment effects on reduced violence risk.

Analysis

The incidence of violence over six 6-month periods (3 years total) was modeled using general linear regression analysis for repeated measures,[64,65] with the probability of violence estimated prospectively as a function of medication type in the previous periods, controlling for time, baseline violence, intensity of mental health services utilization, medication compliance, baseline clinical risk factors, and demographic characteristics. These models are designed to incorporate all available longitudinal data for each subject and to estimate the net association of multiple fixed as well as time-varying predictors of violence, which may covary with, and condition the effects of, the key independent variable (medication type). The models also adjust for lack of independence between observations for each subject over time. Our analysis used a specific procedure designed for an *autoregressive* covariance structure, i.e., a matrix in which the correlation gradually declines between baseline and successive follow-up measures of the dependent variable (violence).

RESULTS

Sample Description

At the time these analyses were conducted, a sample of 124 SCAP subjects in North Carolina taking either olanzapine or risperidone was available with follow-up data sufficient to estimate time-series trends in violence as a function of medication type while controlling for relevant

Table 1. Sample Characteristics at Initiation of Olanzapine or Risperidone

Characteristic	Total N	Olanzapine N	Olanzapine %	Risperidone N	Risperidone %
Demographic characteristics					
Age[a]					
Below median (20–44 y)	63	33	52.38	30	47.62
Median or above (≥ 45 y)	61	26	42.62	35	57.38
Gender					
Female	55	24	43.64	31	56.36
Male	69	35	50.72	34	49.28
Race					
African American	84	40	47.62	44	52.38
White, other	40	19	47.50	21	52.50
Baseline clinical characteristics					
Initial treatment setting					
Inpatient	53	27	50.94	26	49.06
Outpatient	71	32	45.07	39	54.93
Global Assessment of Functioning (GAF)					
Below median (< 35)	74	35	47.30	39	52.70
Median or above (≥ 35)	50	24	48.00	26	52.00
History of substance abuse[a]					
No	99	43	43.43	56	56.57
Yes	25	16	64.00	9	36.00
History of violent behavior[a]					
No	104	46	44.23	58	55.77
Yes	20	13	65.00	7	35.00

[a]Trend toward statistical significance for olanzapine versus risperidone ($p < .10$).

covariates. As described previously, these subjects were enrolled using 2 recruitment strategies simultaneously: sequential inpatient admissions and random selection from community mental health center case rosters. The study was designed with a recruitment goal of obtaining 50% of the sample with a record of hospitalization in the prior year. Of the 124 individuals included in the present analysis, 48% were from the recently hospitalized cohort, while 52% were outpatients who had not been hospitalized within the preceding year.

Regarding gender distribution, 56% of the subjects were male and 44% were female. Age ranged from 20 to 77 years, with a mean of 46.1, a median of 45, and a standard deviation of 12.3 years. With respect to racial background, 67.7% of the subjects were of African American descent and 32.3% were self-identified as white or of other racial/ethnic backgrounds. This demographic distribution fairly reflects the population of consumers with severe mental illness receiving services in the public mental health care system in the north-central region of North Carolina.[60]

Considering clinical status, baseline GAF scores ranged from 10 to 75, with a mean of 35.6, a median of 35, and a standard deviation of 10.9. This distribution indicates that, on average upon enrollment, these subjects were clinically rated as having major impairment in several functional areas such as work, social relations, judgment, and thinking. Twenty percent (20.2%) of the subjects were identified as having co-occurring substance abuse during the 6 months preceding enrollment. Psychotic symptom scores ranged from 1 to 5 with a mean of 2.1, a median of 1.9, and a standard deviation of 1.1. Adverse medication side-effect scores ranged from 1 to 5 with a mean of 1.9, a median of 1.8, and a standard deviation of 0.9.

Refusal and Retention Rates

For the full North Carolina SCAP sample, the baseline refusal rate was 22%; for the current sample of subjects prescribed either olanzapine or risperidone, retention was approximately 75% over 3 years of follow-up. Specifically, retention of subjects declined from 85.9% at 6 months to 74.6% at 36 months. There was no significant association between baseline violence and attrition.

It must be noted that the data presented here represent a subsample of participants—those prescribed olanzapine or risperidone. Thus, only a small proportion of participants from the full sample met selection criteria for the current study. The subset of data that were available for this study included 124 individuals with a combined total of 357 person-period observations distributed as follows: 6 months, N = 80; 12 months, N = 80; 18 months, N = 68; 24 months, N = 74; 30 months, N = 55.

Baseline Association Between Subject Characteristics and Type of Medication Prescribed

Because our design was observational in nature and did not involve random assignment to medication, it was important to examine any preexisting associations between the type of antipsychotic medication prescribed and the subjects' demographic and clinical characteristics. To prevent potential selection biases from yielding misleading results, it was also crucial to statistically control for these baseline characteristics in our multivariable time-series analyses estimating the effects of medication type on violence.

Table 1 presents the frequency distributions resulting from a cross-tabulation of subject characteristics by whether they were initially prescribed olanzapine or risperidone. Of the 124 subjects included in this analysis, 59 had an initial prescription for olanzapine and 65 had an initial prescription for risperidone. Subjects prescribed risperidone did not differ to a statistically significant degree from those prescribed olanzapine. However, the data showed a trend toward differences between groups on age, history of violence, and substance abuse comorbidity; compared to subjects who were prescribed risperidone, those selected for treatment with olanzapine were marginally ($p < .10$) younger, more likely to have a history of violence, and more likely to have a co-occurring substance use disorder.

Prevalence of Violence

At baseline, it was determined that 16.1% of the subjects had committed violent acts in the 6 months prior to

Table 2. Longitudinal Effects of Olanzapine Versus Risperidone Treatment on Violent Behavior in Persons With Schizophrenia, by Duration of Treatment[a]

	Model 1		Model 2	
Independent Variable	OR	95% CI	OR	95% CI
Treatment effects (olanzapine vs risperidone)				
Initiated or switched to olanzapine in past 6 mo [comparison]	[1.00]		[1.00]	
Olanzapine prescribed for past 12 mo or longer	0.30	0.10–0.93*	0.33	0.10–1.10
Initiated or switched to risperidone in past 6 mo	0.49	0.12–2.02	0.56	0.13–2.52
Risperidone prescribed for past 12 mo or longer	0.49	0.17–1.44	0.52	0.17–1.63
Mediating effect of compliance				
Took medication as prescribed "most of the time"			0.43	0.19–0.97*
Correlation between predicted probabilities and observed rates (Somer's D)	0.54		0.53	
Variance explained by model (Pseudo R^2)	0.15		0.16	
	Model 1 compared to intercept and wave only		Model 2 vs Model 1	
χ^2 for improvement of model fit	179.37	(df = 13)***	53.10	(df = 1)***

[a]N = 124 subjects (59 olanzapine-treated, 65 risperidone-treated); no. of observations = 357. Models are adjusted for effects of time (wave), intersubject correlation, outpatient treatment intensity, baseline violence, demographic variables (age, sex, race), baseline clinical variables (hospitalization history, substance abuse, psychotic symptoms, functional impairment), and baseline adverse medication side effects.
Statistical significance: *p < .05; ***p < .001.

enrollment (as identified by MCVI self-report interview, medical record review, civil commitment documents, or arrest records).

Longitudinal Analysis of Medication Type and Violence

As mentioned, a total of 357 person-period observations were available for analysis covering 3 years of follow-up assessments. Table 2 presents the results of a time-series analysis using general estimating equations. These models estimate the longitudinal effects of medication type on reduced violent behavior in the subsequent period, controlling for time and key covariates, as well as adjusting for the nonindependence of repeated measures for individuals (autoregressive covariance structure). Dummy variables were coded for risperidone initiation (switch period), risperidone continuing treatment, olanzapine initiation (switch period), and olanzapine continuing treatment. Olanzapine switch was associated with the highest risk of violence, i.e., "baseline" violence at the time of switch was highest in those prescribed olanzapine. Hence, this group was used as the comparison group for the other 3 groups in the analysis. Compliance with medication and mental health service intensity were included as separate time-varying covariates, while baseline violence, demographic characteristics, and clinical risk factors were included as controls.

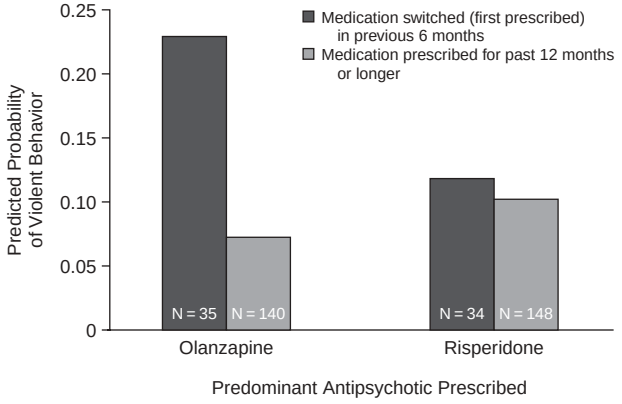
Model 1 shows a significant main effect of reduced incidence of violence associated with remaining on olanzapine treatment for 12 months or longer (OR = 0.30, p < .05). This model also included controls for a number of salient variables (not shown): baseline violence (OR = 4.24, p < .01), outpatient mental health service intensity, demographic variables (age [OR = 0.97, p < .10], sex, race), baseline clinical variables (hospitalization history, substance abuse, psychotic symptoms, functional impairment), and baseline adverse medication side effects (OR = 1.75, p < .05).

Model 2 added a term for medication compliance while still controlling for the covariates listed. In this model, several covariates (not shown) were significantly associated with violence. Specifically, compliance with prescribed medication "most of the time" or "all of the time" was significantly associated with reduced violence (OR = 0.43, p < .05). Baseline violence remained significant in predicting subsequent violence (OR = 4.34, p < .01), as did baseline adverse medication side effects (OR = 1.63, p < .05).

In model 2, the introduction of medication compliance as a covariate rendered nonsignificant the main effect of being on olanzapine therapy for 12 months or longer, even though the odds ratio remained quite low (OR = 0.33, p = .07). This finding suggests that medication compliance may function as a mediating effect in the relationship between sustained treatment with olanzapine and reduction of violent behavior. In order to further explore this possibility, a model predicting medication compliance was estimated (model not shown). In this model, we found a statistical trend toward greater compliance with medication among those subjects who remained on olanzapine therapy for 12 months or longer, compared to initiation period (OR = 1.94, p = .07). No such trend was found for those subjects remaining on risperidone therapy for the same amount of time (OR = 1.11, p = .79).

Finally, Figure 1 illustrates the predicted probabilities of violent behavior by duration and type of treatment, controlling for the variables included in model 2 of Table 2. Figure 1 shows that subjects prescribed olanzapine had a reduced probability of violence over time (0.229 to 0.071); however, the same was not true for those subjects taking risperidone (0.118 to 0.101).

Figure 1. Probability of Any Violent Behavior in 6 Months Among Patients Prescribed Olanzapine Versus Risperidone, by Duration of Treatment



DISCUSSION

In this article, we report new findings from a longitudinal, observational study of violent behavior among persons with schizophrenia in the community, comparing the effects of treatment with olanzapine versus risperidone in reducing violence risk over time. In a previous report from this study,[27] we found that treatment with atypical antipsychotics, as a class (clozapine, risperidone, or olanzapine), was associated with significant reduction of violence risk over time, whereas conventional antipsychotic agents did not significantly reduce violence. This positive impact for atypicals was at least partially an indirect effect, being mediated by concurrent reductions in medication side effects, substance abuse, and psychotic symptoms. The effect was also found to interact statistically with medication adherence, i.e., the impact of atypicals was greatest among patients who reportedly were taking their medications as prescribed at least "most of the time."[27] In the present study, we conducted multivariable time-series analyses, controlled for salient demographic and clinical covariates, and found that patients who remained on olanzapine treatment for 1 year or more had significantly lower violence risk compared to the first period when switched to the new drug. However, no significant change in violence risk was found for subjects remaining on risperidone treatment for 1 year or more. Adherence with prescribed medication was found to mediate the association between olanzapine treatment and reduced violent behavior.

To our knowledge these are the first studies examining the effects of atypical antipsychotic regimens on violence risk in naturalistic settings. We find, in the complex "real world" settings where persons with schizophrenia reside, that long-term treatment with olanzapine confers some advantage over risperidone in reducing violence risk. This advantage appears to be at least in part an indirect effect, via improvement in adherence with treatment. Due to the limitations in sample size, we were not able to compare the potential effects of these 2 medications on concomitant reductions in psychotic symptoms, co-occurring substance abuse, and adverse side effects of medication—other potential mediators of the complex relationship between treatment with atypicals, better adherence, and lower violence risk.

The apparent advantage conferred by olanzapine could be attributable to its somewhat different pharmacologic profile compared with risperidone, including differences in serotonergic or other receptor activity, side-effect profile, sedating properties, or overall tolerability. The current study cannot shed more light on many of these potential differences between these medications. However, the present data suggest one pathway to reduced violence risk is via improved medication adherence—possibly indicating an advantage of olanzapine in tolerability at the doses and dosing intervals in common use in the community.

We also find that baseline violent behavior and adverse medication side effects are independent predictors of subsequent violence and that these effects persist after medication compliance is controlled in multivariable analysis. Numerous studies of violence among psychiatric patients have found that a history of violence is a robust predictor of subsequent violence.[12,59] This suggests that some persons with schizophrenia—particularly those exposed to violence over their life course—are predisposed to violent behavior; pharmacologic or psychosocial treatment may modify, but not eliminate, their risk of violence. In this population, violent behavior is also associated with comorbid substance use and noncompliance with treatment.[8,9] To some extent, baseline violence may also be a proxy for these co-occurring problems, which are often very difficult to assess.

Baseline adverse side effects—such as dysphoria or persistent extrapyramidal symptoms—could be a direct cause of violence in some patients, but may also lead to violence indirectly by impeding medication adherence. Conversely, reduced extrapyramidal symptoms and other adverse side effects may lead to improved compliance, reduced psychotic symptoms, diminished substance abuse, increased participation in other supportive outpatient services, and ultimately improved social functioning—all of which, in turn, may help prevent assaultive behavior.[38]

Given the observational design of this study and the absence of random assignment to treatment conditions, it is possible that selection bias could affect these results, e.g., if "less problematic" patients with lower violence risk were differentially selected for treatment with olanzapine over risperidone. However, this does not appear to be the case. Specifically, there was a trend for those subjects prescribed olanzapine to be younger, more violent, and to

have a co-occurring substance abuse disorder ($p < .10$) at baseline assessment, compared to their counterparts who were prescribed risperidone. That is to say, it appears that more violence-prone subjects were initially switched to olanzapine. Therefore, if there is a selection bias associated with the prescription of either olanzapine or risperidone and risk for future violence, then such a bias would here seem to work *against* finding that olanzapine lowers the risk of violence. Thus, our results may even understate the true impact of olanzapine in preventing violent behavior. Nonetheless, there could be other unknown selection factors at work that may have differentially selected patients for olanzapine versus risperidone and biased these results. Confirmation of these findings awaits a more definitive controlled trial, such as the National Institute of Mental Health Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) project,[66] which is currently in the field.

Drug names: clozapine (Clozaril, Fazaclo, and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), ziprasidone (Geodon).

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