Pathways to Violent Behavior During First-Episode Psychosis
A Report From the UK National EDEN Study

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**IMPORTANCE** Although many studies have explored the correlates of violence during first-episode psychosis (FEP), most have simply compared violent psychotic individuals with nonviolent psychotic individuals. Accumulating evidence suggests there may be subgroups within psychosis, differing in terms of developmental processes and proximal factors associated with violent behavior.

**OBJECTIVE** To determine whether there are subgroups of psychotic individuals characterized by different developmental trajectories to violent behavior.

**DESIGN, SETTING, AND PARTICIPANTS** The National EDEN (Evaluating the Development and Impact of Early Intervention Services in the West Midlands) Study longitudinal cohort assessed premorbid delinquency (premorbid adjustment adaptation subscale across childhood and adolescence), age at illness onset, duration of untreated psychosis, past drug use, positive symptoms, and violent behavior. Group trajectories of premorbid delinquency were estimated using latent class growth analysis, and associations with violent behavior were quantified. This study included 6 early intervention services in 5 geographical locations across England, with violent behavior information available for 670 first-episode psychosis cases.

**MAIN OUTCOMES AND MEASURES** Violent behavior at 6 or 12 months following early intervention services entry.

**RESULTS** Four groups of premorbid delinquency were identified: stable low, adolescent-onset high to moderate, stable moderate, and stable high. Logistic regression analysis, with stable low delinquency as the reference group, demonstrated that moderate (odds ratio, 1.97; 95% CI, 1.12-3.46) and high (odds ratio, 3.53; 95% CI, 1.85-6.73) premorbid delinquency trajectories increased the risk for violent behavior during FEP. After controlling for confounders, path analysis demonstrated that the increased risk for violence in the moderate delinquency group was indirect (ie, partially mediated by positive symptoms) (probit coefficient β = 0.12; P = .002), while stable high delinquency directly increased the risk for violence (β = 0.38; P = .05).

**CONCLUSIONS AND RELEVANCE** There appear to be diverse pathways to violent behavior during FEP. Stable high premorbid delinquency from childhood onwards appears to directly increase the risk for violent behavior, independent of psychosis-related risk factors. In addition to tackling illness-related risks, treatments should directly address antisocial traits as a potent risk for violence during FEP.
Recent studies suggest that the first-episode of psychosis (FEP) may represent a period of heightened risk for violence. Most studies examining the correlates of violence during FEP consider violent psychotic individuals as a homogeneous group (i.e., compare all violent psychotic individuals with nonviolent psychotic individuals). Accumulating evidence does not support this assumption. Moffitt and Caspi identified subgroups of nonmentally ill offenders, defined by age at onset and persistence of antisocial behavior. It is likely that similar subgroups exist among violent individuals with psychosis. The presence of subgroups may explain apparent inconsistencies within the literature (e.g., the inconsistent association between positive symptoms and violence during psychosis).

Furthermore, understanding unique trajectories of violent behavior predating and following the onset of psychosis can increase understanding regarding drivers of violence, help identify at-risk groups, and inform treatment approaches to reduce violence.

It has been hypothesized that there are 3 groups of violent psychotic individuals. The early starters display a pattern of antisocial behavior emerging in childhood, which remains relatively stable across the lifespan. The second group displays no antisocial behavior prior to illness, then repeatedly engages in aggressive behavior. The third displays no antisocial behavior prior to and for the first few decades of illness, then commits serious violence. Congruent with the developmental taxonomy of antisocial behavior, which proposes 2 primary hypothetical prototypes—life-course persistent and adolescence limited—the early starters likely represent the former of the 2 groups. These individuals display a tendency toward antisocial behavior prior to the onset of psychosis, which culminates in a personality disorder in addition to the psychosis.

Evidence for the early starter vs illness onset hypothesis is beginning to accumulate. Conduct disorder before age 15 years is an antecedent of psychosis. In a prospective study, 40% of individuals who developed schizophrenia by age 26 years displayed conduct disorder prior to the age of 15. Furthermore, patients with severe mental illness and a history of conduct disorder by midadolescence were at increased risk for violent behavior, after controlling for substance abuse. Swanson and colleagues found that clinical correlates of violence in patients with schizophrenia varied according to premorbid conduct problems or acute psychopathology course (i.e., an association between positive symptoms and violence was only observed in the acute psychopathology group). They concluded that violence among adults with schizophrenia may follow at least 2 pathways. To our knowledge, there are no existing studies that simultaneously delineate direct and indirect (i.e., mediated) pathways from past conduct problems to violent behavior during FEP.

Studies have explored the associations between premorbid adjustment, assessed using the Premorbid Adjustment Scale (PAS), and course of psychotic illness, although not patterns of violent behavior specifically. Cole et al. identified 3 distinct groups of premorbid functioning (poor deteriorating, insidious onset, and good stable) using latent class growth analysis (LCGA), distinguishable in terms of age at illness onset, processing speed, and functioning after onset. Because it is likely that violence during psychosis may follow at least 2 distinct pathways, we adopted a similar approach. Using LCGA, we sought to identify distinct groups of individuals based on premorbid adaptation (i.e., delinquency) patterns across childhood and adolescence, and we explored the pathways (direct and indirect) from premorbid delinquency to violent behavior during FEP. We used the PAS adaptation to school subscale (i.e., denoting discipline problems and delinquent behavior) as a proxy marker for conduct problems. We aimed to answer the following questions:

1. Do FEP patients have distinct subgroups, characterized by different trajectories of delinquency across childhood and adolescence?
2. Do these subgroups differ in terms of prevalence of violent behavior following early intervention service (EIS) entry?
3. What are the direct and indirect (i.e., mediated [via other risk factors for violence, i.e., past drug use, duration of untreated psychosis, positive symptoms, age at onset of illness]) associations between premorbid delinquency groups and violent behavior following EIS entry?

### Methods

#### Sample

We analyzed data from the National EDEN (Evaluating the Development and Impact of Early Intervention Services in the West Midlands) Study, a longitudinal cohort of patients managed by 6 EISs in 5 locations across England: Birmingham, Cornwall, Cambridge, Norwich, and Lancashire. All individuals with FEP and enrolled into the EIS were approached for recruitment from August 1, 2005, to April 30, 2009. Entry criteria for EISs were standardized and consistent among sites because their commissioning resulted from a national policy implementation guide. Participants within the ultra-high-risk group were explicitly excluded because they were not part of the EIS protocol. Patients comprised the broad spectrum of nonaffective psychosis and were assessed at baseline (entry into EIS) and at 6 and 12 months by researchers not directly involved in clinical care. Numerous assessments (e.g., psychotic symptoms and premorbid functioning) were administered at each point. Before each assessment, participants in the study were explicitly informed that while information and data collected were confidential, researchers may disclose concerns about serious risk to self or others to the treating clinical team. Comprehensive ethical approval for this study was granted by the South West Multicentre Research Ethics Committee.

A total of 1,027 individuals consented to the study (50% of those approached; see article by Birchwood et al. for information on nonresponders). The violent behavior outcome was available at both points for 670 individuals (65% of the consented group). Attrition analyses revealed those with violent behavior outcome data did not significantly differ from those who originally consented to the study (eTable 1 in Supplement).

#### Measures

Violent behavior was assessed at 6 and 12 months using the Adverse Outcomes Screening Questionnaire, a shortened ver-
sion of the MacArthur study questionnaire, modified for use in the United Kingdom.29 Individuals were asked whether they had physically harmed others in the last 6 months. If they replied yes at either point, they were coded as being violent following EIS contact (0 = no violent behavior; 1 = any violent behavior) and then asked further questions regarding how often, who they harmed, and in what way (eg, used a knife).

Premorbid delinquency was measured via self-report using the PAS during baseline assessment.18 Individuals were asked about premorbid adaptation to school during childhood (up to age 11 years), early adolescence (age 12-15 years), and late adolescence (age 16-18 years). At each point, possible responses were: good adaptation (0 points; ie, enjoys school, no or rare discipline problem, has friends at school, and likes most teachers), fair adaptation (1-2 points; ie, occasional discipline problem, not very interested in school but no or rare truancy, and has friends at school but does not often take part in extracurricular activities), poor adaptation (3-4 points; ie, dislikes school, frequent truancy, and frequent discipline problem), and refuses to have anything to do with school (5-6 points; ie, delinquency or vandalism directed against the school). Responses to the adaptation scale for childhood, early adolescence, and late adolescence were entered as continuous indicator variables in the LCGA (see Analysis Methods section).

Potential Confounders

Drug Use and Duration of Untreated Psychosis
Past drug use was self-reported at baseline (0 = no past drug use; 1 = not more than 3 times; 2 = less than weekly; 3 = 1 to 3 times weekly; 4 = almost every day). Duration of untreated psychosis (DUP) was defined as the delay between the onset of psychosis and the onset of criteria treatment and was calculated using a robust strategy (for more information, see article by Birchwood et al14). A dichotomous DUP variable was constructed representing short (0 = <6 months) and long (1 = >6 months) DUP.1

Male Sex, Positive Symptoms, and Younger Age at Illness Onset
Male sex is associated with antisocial behavior from childhood onwards.19 Therefore, sex (male = 69%; female = 31%) was controlled for when estimating trajectories of premorbid delinquency.

Positive symptoms were assessed at 6 months using the Positive and Negative Syndrome Scale.20 The 6-month measure was chosen to ensure that positive symptoms were in close temporal proximity2 with the violent outcome. Age at onset of illness was reported at baseline (mean [SD], 21.33 [4.98] years).

Analysis Methods

LCGA: Trajectories of Premorbid Delinquency

Latent class growth analyses were conducted using Mplus21 version 6. Latent class growth analysis has become popular for its use in identifying homogeneous groups of subpopulations. The indicator variables were PAS adaptation scores (ie, delinquency) for childhood, early adolescence, and late adolescence. Several models were fitted by increasing the number of classes.22 Owing to the robust link between antisocial behavior and sex,5 sex was included as a covariate. The best-fitting classification model was chosen according to fit indices (ie, Bayesian Information Criteria [BIC] and Vuong-Lo-Mendell-Rubin [VLMR] test) and consideration of the meaningfulness of the successive models.22 Lower BIC values suggest better model fit. A significant VLMR value suggests that a K-class model fits the data better than a (K-1) class model (ie, an additional class improves model fit).22

Premorbid Delinquency Groups and Risks for Violence and Violent Behavior During FEP

The estimated premorbid delinquency classes were saved and imported into SPSS for further analysis.22 Crude associations between premorbid delinquency class and risk factors for violence (eg, positive symptoms) and violent behavior following EIS entry were assessed. Associations with dichotomous outcomes were quantified using logistic regression analysis, yielding odds ratios (ORs) with 95% CIs. Mean differences in continuous outcomes were tested using analysis of variance.

Direct and Indirect Associations Between Premorbid Delinquency Groups and Violent Behavior During FEP

Path analyses were conducted using Mplus21 version 6. Variables were entered according to time ordering of assessment. Premorbid delinquency classes (adolescent-onset high-to-moderate, stable moderate, and stable high delinquency, with stable low delinquency as the reference group) were entered as independent variables; DUP, drug use, and positive symptoms were entered as independent, mediator, and outcome variables. Violent behavior was the main outcome variable (Figure 1). The weighted least squares with robust standard errors and mean- and variance-adjusted estimator were used for their robustness when analyzing continuous and categorical outcomes.23

Results

Latent Classes of Premorbid Delinquency

Table 1 shows the values of log-likelihood (VLMR), BIC, and number of parameters for all models assessed. Overall, a 4-class model offered the best fit. It had the second-lowest BIC value, and the VLMR P value suggested that it represented a significantly better fit than the 3-class model. While the 5-class model had a lower BIC value, this model produced 2 very similar classes in terms of intercept and slope (which could be subsumed under the stable moderate subgroup).

The 4 derived classes of premorbid delinquency are presented in Figure 2: stable low delinquency (48.5%); stable moderate delinquency (28.7%); stable high delinquency (13.2%); and early adolescent-onset high-to-moderate delinquency (9.7%). Male sex was significantly associated with moderate and high delinquency class using the stable low class as the reference group: moderate (OR, 1.81; 95% CI, 1.22-2.69) and high (OR, 2.36; 95% CI, 1.41-3.95) premorbid delinquency.

Premorbid Delinquency Classes, Risk Factors for Violence, and Violent Behavior Following EIS Entry

Following EIS entry, 13.7% (8.6% at 6 months; 8.5% at 12 months) of the total sample were violent at 6 or 12 months (for
details on violent acts, see eTable 2 in Supplement). The following reported violent behavior: 8.7% of the stable low group, 9.3% of the early adolescent–onset group, 15.5% of the stable moderate group, and 25.3% of the stable high group. Compared with the stable low group, those in the moderate delinquency group were twice as likely (OR, 1.97; 95% CI, 1.12-3.46) to report violence, and the stable high delinquency group was 3.5 times more likely (OR, 3.53; 95% CI, 1.85-6.73) to report violence.

Premorbid delinquency groups (with low delinquency as the reference) were associated with all risk factors for violent behavior. Moderate (OR, 1.75; 95% CI, 1.27-2.40) and high (OR, 2.29; 95% CI, 1.52-3.43) delinquency groups were significantly associated with longer DUP. Delinquency class was significantly associated with past drug use: adolescent onset (2.44 vs 1.64; \(P = .001\)), moderate (2.24 vs 1.64; \(P < .001\)), and high (2.48 vs 1.64; \(P < .001\)). Moderate (12.64 vs 10.52; \(P < .001\)) and high (12.31 vs 10.52; \(P = .002\)) delinquency groups had higher mean positive symptom scores. All higher premorbid delinquency groups had a younger age at illness onset: adolescent onset (20.04 vs 22.08; \(P = .007\)), moderate (20.68 vs 22.08; \(P = .002\)), and high (20.42 vs 22.08; \(P = .006\)).

Past drug use (OR, 1.15; 95% CI, 1.00-1.32), longer DUP (OR, 1.66; 95% CI, 1.06-2.58), positive symptoms (OR, 1.15; 95% CI, 1.09-1.21), and younger age at illness onset (OR, 0.91; 95% CI, 0.87-0.96) were all significantly associated with violent behavior.

**Direct and Indirect Associations With Violence**
A path model was estimated to simultaneously include all the risk factors for violence and quantify direct and indirect pathways to violent behavior. This model yielded a good fit:\(^2 \chi = 6.46; P = .09\); root mean square error of approximation = 0.04; Comparative Fit Index = 0.98. The main direct and indirect associations are shown in Table 2. Associations are reported in unstandardized probit coefficients for dichotomous outcomes (ie, a probit coefficient of 0.08 indicates that for each unit increase in the positive symptoms scale, there was an increase of 0.08 SDs in the predicted \(z\) score of the cumulative normal distribution of violent behavior).\(^{25}\) Associations for continuous outcomes are reported as linear regression coefficients.

Stable high premorbid delinquency, positive symptoms, and younger age at illness onset were independently associated with violent behavior following EIS entry (Table 2). Duration of untreated psychosis was associated with positive symptoms (\(\beta = 0.93\); standard error [SE] = 0.20; \(P < .001\)) and indirectly predicted violence via positive symptoms (Table 2). Adolescent-onset (\(\beta = 0.77\); SE = 0.30; \(P = .009\)), stable moderate (\(\beta = 0.44\); SE = 0.16; \(P = .006\)), and stable high (\(\beta = 0.76\); SE = 0.22; \(P = .001\)) premorbid delinquency were associated with past drug use; and higher delinquency (\(\beta = 0.33\); SE = 0.16; \(P = .04\)) with longer DUP. Adolescent-onset (\(\beta = -2.55\); SE = 0.84; \(P = .002\)), stable moderate (\(\beta = -1.60\); SE = 0.46; \(P < .001\)), and stable high (\(\beta = -1.78\); SE = 0.66; \(P = .007\)) premorbid delinquency had a younger age at illness onset. There was an indirect association between stable moderate delinquency and violence via positive symptoms (Table 2).

**Discussion**
We explored whether individuals during FEP may be meaningfully subdivided according to premorbid levels of delinquency.
quent behavior across childhood and adolescence. Using LCGA, we identified 4 distinct groups, 3 of which demonstrated relatively stable patterns of delinquency over time. These can be described as stable low delinquency, stable moderate delinquency, and stable high delinquency. The fourth group displayed a pattern of low delinquency in childhood, peaking in early adolescence then gradually declining, described as early adolescent–onset high-to-moderate delinquency.

Crude analyses suggested that the prevalence of violent behavior following EIS entry was significantly higher among patients with moderate and high premorbid delinquency, although not for those with adolescent-onset delinquency. These findings are consistent with the developmental theory of antisocial behavior (ie, life-course persistent vs adolescence limited), suggesting that similar patterns of antisocial behavior may be found in psychotic patients. An appreciable number of individuals (8.7%) reporting low premorbid delinquency were violent following EIS entry, demonstrating an additional pathway to violence during FEP, in which antisocial behavior is initiated for the first time following illness onset.

Using path analysis, associations between premorbid delinquency trajectories, risk factors for violence and violent behavior following EIS entry, were simultaneously assessed. Within this model, stable high delinquency, positive symptoms, and age at illness onset were all directly associated with violent behavior after controlling for all risk factors for violence. It is of particular note that high delinquency was independently associated with violent behavior. The high delinquency group trajectory, which reflected consistently high levels of delinquent behavior across childhood and adolescence, may have captured the early starters suggested in previous research. Thus, the continuance of antisocial tendencies may have accounted for the increased risk for violent behavior in this group. Research suggests that psychotic patients with comorbid personality disorder are more likely to behave violently and may require treatments over and above those for positive symptoms and substance abuse (ie, psychosocial treatments). Nevertheless, while there are clinical guidelines for the short-term management of violent behavior in inpatient settings (ie, tranquilization and physical intervention), there are no treatment recommendations for specifically targeting chronic violent behavior. This may explain, in part, why rates of aggression during FEP appear not to alter substantially following service contact.

While in crude analyses, moderate premorbid delinquency increased the risk for violence during FEP, it was not independently associated with violence once all risk factors were controlled for. The path analysis suggested the increased risk was partially mediated by positive symptoms (ie, moderate pre-
Morbidity delinquency was associated with higher positive symptom scores, which were associated with an increased risk for violent behavior. Thus, moderate premorbid delinquency may represent a general risk marker for poorer outcome rather than a specific risk marker for violent behavior. Indeed, those in the moderate delinquency group were more likely to report past drug use and earlier illness onset and experience longer DUP compared with those in the stable low group. In a previous study, positive symptoms were only associated with violent behavior in the patient group without a history of conduct problems. Our results are consistent with these findings, demonstrating that positive symptoms may mediate the association between moderate delinquency and violent behavior, but not high delinquency and violent behavior.

Congruent with previous reports, we found a main effect of positive symptoms on violent outcome. In a recent meta-analysis, positive symptoms were not significantly associated with violence during FEP; however, there were inter-study inconsistencies regarding the temporal relationship between positive symptoms and episodes of violence. In our study, the assessment of positive symptoms was close in temporal proximity to the violent behavior. An indirect association between longer DUP and violent behavior via positive symptoms was observed. Previous studies reported that longer DUP is associated with positive symptoms and violence during FEP; the results here expand this work by suggesting that positive symptoms may be one underlying mechanism via which longer DUP increases the risk for violence during FEP.

Study strengths include the large sample size, prospective assessment of various risk factors for violence across points, and the use of a variety of statistical procedures. Latent class growth analysis facilitated the subdivision of a heterogeneous group of psychotic individuals into meaningful homogeneous subgroups, while path analysis facilitated the modeling of direct and indirect associations simultaneously.

There were also a number of limitations. Only 50% of the individuals with FEP approached agreed to participate in the study; 65% of whom had violent behavior measures. Therefore, the analysis sample represents 33% of the original sample. Although attrition analysis supports that those lost to follow-up did not significantly differ in terms of premorbid history and risk factors for violence, we could not assess differences for those who refused to take part in the study. Therefore, it is possible that this study underestimates the prevalence of violent behavior because individuals with higher premorbid delinquency may have been less likely to participate in the study or may have been in prison. Second, retrospective informant-report measures were used for information regarding premorbid functioning. While retrospective reports are not ideal, research supports the predictive and concurrent validity of the PAS School Adaptation Scale, which yielded similar developmental trajectories to those reported in the antisocial behavior literature. Furthermore, the derived groups demonstrated meaningful associations with important outcomes. Third, violent behavior was self-reported, potentially leading to bias; however, self-report of violent acts has the benefit of detecting acts that may otherwise remain unknown. Fourth, baseline data on alcohol use was not available; therefore, we could not control for this risk factor. Because alcohol and drug abuse often co-occur, some of this risk may have been accounted for by reported drug use; nevertheless, future studies should consider whether alcohol abuse specifically, distinguishes pathways to violence during FEP. Finally, although care was taken to preserve the time ordering of risk factors for violence, violent behavior was assessed at both 6 and 12 months, while positive symptoms were assessed at 6 months. Therefore, it is possible that in some cases, violent behavior may have preceded positive symptoms.

Our findings suggest there are several distinct pathways to violent behavior during FEP. Individuals displaying antisocial behavior from childhood onwards may be especially likely to engage in violent behavior during FEP. Future studies may consider whether pathways to violence during FEP vary according to sex, environmental premorbid risk factors (eg, childhood trauma), and severity of violence. Early intervention strategies should target antisocial traits, and treatment approaches should focus simultaneously on the psychotic disorder and violent behavior. Furthermore, international guidelines should include information on evidence-based treatment options for violence during psychosis.
Violent Behavior During First-Episode Psychosis

Research through the Collaborations for Leadership in Applied Health Research and Care for Birmingham and Black Country. No other disclosures were reported.

Funding/Support: This work was funded by the United Kingdom Department of Health’s (grant PO261680) A National Evaluation of Early Intervention for Psychosis Services: DUP, Service Engagement and Outcome (the National EDEN Project) to Drs Lester and Birchwood.

Role of the Sponsor: The funding agency had no role in design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

Disclaimer: The views expressed in this article are not necessarily those of the National Institute for Health Research, the United Kingdom Department of Health, the University of Birmingham, or the Collaborations for Leadership in Applied Health Research and Care for Birmingham and Black Country theme 3 management group.

Additional Information: We thank Dr Lester, our highly esteemed friend and colleague who died during the production of this article.

REFERENCES


