Insight as a Predictor of the Outcome of First-Episode Nonaffective Psychosis in a Prospective Cohort Study in England

Richard J. Drake, M.R.C.Psych., Ph.D.; Graham Dunn, Ph.D.; Nick Tarrier, Ph.D.; Richard P. Bentall, Ph.D.; Gillian Haddock, Ph.D.; and Shôn W. Lewis, F.R.C.Psych.

Objective: To estimate the effect of insight on time to relapse and readmission and on social function and symptoms after following up a cohort of first-episodes of nonaffective psychosis for 18 months.

Method: Patients with first episodes of DSM-IV schizophreniform disorder, schizophrenia, schizoaffective disorder, delusional disorder, and psychosis not otherwise specified (excluding primary substance-induced or organic psychoses), aged 16 to 65 years, were recruited over the 26 months from July 1996 to September 1998 from consecutive admissions to day-patient and inpatient units in England with a catchment area population of 2.3 million. They were interviewed with the Positive and Negative Syndrome Scale, Birchwood Insight Scale, and Social Functioning Scale at baseline and 18 months.

Results: The hazard ratio for relapse, per unit increase in the insight score, was estimated in a Cox proportional hazards model to be 0.943 (95% CI = 0.892 to 0.996; p = .035). Those with the best insight scores had an estimated rate of relapse that was 39% of that of those with the worst scores (95% CI = 16% to 93%). Readmission was highly correlated with relapse, so poor insight also predicted readmission (hazard ratio 0.934; 95% CI = 0.876 to 0.996; p = .036). However, insight did not independently predict symptoms or social function after adjustment for other predictors of outcome.

Conclusion: Insight predicted both relapse and readmission. The details of the beliefs and assumptions determining outcome remain unclear, but intervening to alter them appears to be justified.

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Corresponding author and reprints: Richard J. Drake, M.R.C.Psych., University of Manchester Division of Psychiatry, 2nd Floor, Education & Research Centre, Wythenshawe Hospital, Manchester, M23 9PL, UK (e-mail: richard.drake@manchester.ac.uk).

The determinants of outcome in schizophrenia are still poorly understood. An important way to study them is to follow up first-episode cohorts. This allows detailed assessment of the clinical features and course of a whole range of patients at approximately the same stage of illness. Ideally, consecutive contacts from a defined period and catchment area are recruited prospectively. Existing first-episode studies now extend to between 15 and 25 years: Harrison et al.[1] examined the cohort of contacts with first episodes of nonaffective psychosis from the World Health Organization Determinants of Outcome of Severe Mental Disorders study.[2] Initial 2-year course and country predicted level of symptoms at 15-year follow-up. In some analyses, diagnosis and age at onset also predicted symptoms. Course, country, diagnosis and—again in certain analyses—negative symptoms at onset, "street" drug use, and family support predicted social function.

Smaller, medium-term studies have often also found negative symptoms,[3–8] male sex,[4,5,9] poor social function at presentation[4–8] and sometimes young onset[7] and duration of untreated psychosis[10–12] predicted poor outcome. However, findings are inconsistent,[11–13] in part because of differences in sample sizes and sources and differences in measures and analyses. First-episode patients are difficult to trace, and it is often unclear how dropout biased outcome.

No first-episode study has yet included poor insight as a predictor, despite its clinical relevance to managing illness, although one study of early psychosis patients found that a symptom factor related to insight predicted readmission but not other outcomes.[14] Poor insight is a distinct aspect of psychopathology[14,15] that may be more impaired in first-episode than in chronic psychosis.[16] The balance of evidence favors insight as an important determinant of adherence to medication after first episodes of psychosis, adherence itself being a critical determinant of risk of relapse.[13]

Definitions of poor adherence vary, but 42% to 59% of first-episode patients have irregular adherence or less in naturalistic cohorts followed up for 1 year or more.[17–20] Samples with longer follow-up or those limited to schizophrenia tend to have fewer continuously adherent participants. All multivariate analyses of first-episode samples including insight show it predicts adherence,[21–24] except that of Coldham et al.[20] They found the basic association significant, but this disappeared in a logistic regression including premorbid function, family involvement, concurrent cannabis use, and age.

In samples of patients with more chronic disease, poor insight appears to predict several forms of poor outcome,[25] and there is evidence for several mechanisms apart from adherence.[26] These include poor engagement with rehabilitation,[27] greater propensity to engage in risky behaviors like substance abuse,[28] and failure to act appropriately on early warning signs of relapse.[29] Impaired insight is probably associated with neuropsychological impairment.[30]

We aimed to test the hypothesis that, for people with first episodes of nonaffective psychosis, insight independently influences time to relapse, readmission, and symptoms and social function after 18 months. We used a sample recruited into a trial of cognitive-behavioral psychotherapy.[31,32] We anticipated that relapse and readmission would be related but not necessarily symptoms and social function.

METHOD

Subjects

The sample was a first-episode subsample of a randomized controlled trial that showed cognitive-behavioral therapy during the acute episode made small improvements to symptoms at 18 months but did not affect time to relapse.[31,32] All consecutive first admissions with DSM-IV schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, or psychotic disorder not otherwise specified, aged 16 to 65 years, over a 26-month period from July 1996 to September 1998 to day-patient and inpatient units were approached within 14 working days of admission. The catchment area was defined around 3 centers (defined geographical areas containing a range of National Health Service units) in England with a total population of 2.3 million. Exclusion criteria were organic brain disease, primary substance-induced psychosis, or insufficient capacity to consent. Local research ethics committees for each site approved the study. After complete description of the study to the subjects, written informed consent was obtained.

Predictors

We included a range of potential confounders, but patient allocation to therapy group for the trial was by a fundamentally random process,[31] so it would therefore not be a confounder in these analyses, and it was not included. Demographic data and "baseline substance abuse" (daily illicit drug use or meeting DSM-IV alcohol dependence criteria at the point of admission) were recorded. Diagnosis was made at baseline by clinician raters, by consensus with S.W.L. if there was uncertainty. Diagnosis was reassessed at 18 months by consensus, using symptom ratings and case notes.

Duration of untreated psychosis was calculated from the date of first positive psychotic symptoms to the start of antipsychotic drug treatment, according to an algorithm based on interview with patients, staff, and, where possible, relatives. The most conservative estimate was used for each source, with the longest estimate and patient account given most weight (usually both were the same), provided they were consistent with external evidence.[33] Duration of untreated psychosis was normalized with a logarithmic transformation.

Symptoms and Disability

The Positive and Negative Syndrome Scale for schizophrenia (PANSS)[34] was completed at baseline. One week later the Birchwood Insight Scale (BIS),[35] an 8-item self-completed schedule (see Appendix 1), and Social Functioning Scale (SFS)[36] were completed. After 6 weeks the Drug Attitudes Inventory (DAI)[37] was completed.

Outcome Measures

Symptoms and disability. After 18 months the PANSS, BIS, and SFS were repeated.

Relapse. After final interviews, medical notes were rated independently of the rater in that center to determine the dates of relapse. This was defined as an exacerbation of positive symptoms lasting at least 2 weeks, leading to a change in management (such as increase in medication or admission to hospital). Interrater reliabilities were calculated for whether a relapse had occurred ($\kappa = 0.72$) and time to relapse (intraclass correlation = 0.69).

Rehospitalization. Dates were obtained from the National Health Service hospitals in the catchment areas. Use of non–National Health Service facilities was negligible.

Statistical Analyses

All significance tests were 2-tailed, and all confidence intervals were 95% and 2-tailed. SPSS 11.0.1[38] was used for all routine data analyses and for fitting the Cox proportional hazards models. Mplus 3.12[39] was used to fit simultaneous multiple regression models for quantitative outcomes.

Separate Cox regressions were performed to model (a) survival without relapse and (b) survival without rehospitalization. The baseline BIS total score was the key potential predictor, its effects being estimated after adjusting for the potentially confounding effects of ethnic group, sex, age, years of full-time education, diagnosis, substance misuse, $\log_{10}$(duration of untreated psychosis), baseline PANSS total score, baseline PANSS negative subtotal score, and baseline SFS total score. All analyses were stratified by treatment center because differing services at different centers might have altered rehospitalization rates, in turn affecting when relapse was detected.

The effects of insight (baseline BIS total score) on both symptom severity (PANSS total score) and social functioning (SFS score) were estimated through simultaneously fitting 2 multiple regression models (both including the above potential confounders and treatment center in the regression) in Mplus. Missing outcome data were assumed to be ignorable in Little and Rubin's terminology.[40] Missing baseline measures (of BIS and SFS scores) were also present, but as long as being missing is unrelated to outcome, an analysis based on participants without missing baseline covariates should not yield biased results.[41,42]

RESULTS

Completed Sample and Dropouts

257 patients were recruited after 40 (13%) refused or could not consent. At 18-month follow-up, 72% were reinterviewed. All participants provided data on treatment center, ethnic group, sex, diagnosis, substance misuse, and PANSS scores. Two had missing data for duration of untreated psychosis and 3 had missing values for age and years of full-time education. There were 60 participants who failed to provide a baseline insight (BIS) score and 63 who failed to provide a baseline SFS score (56 had missing values for both measures). There was also attrition (dropout) during the 18-month follow-up, with 71 participants failing to provide an 18-month PANSS score and 99 failing to provide an 18-month SFS score (70 had missing data for both outcomes). Table 1 compares participants who provided an 18-month SFS score (completers) with those who did not. On logistic regression only treatment center differed significantly between completers and noncompleters ($p = .032$).

When rediagnosed after 18 months, 243 patients (95%) still met initial inclusion criteria. The 14 patients (5%) with final diagnoses outside inclusion criteria included 4 with primary substance-induced psychoses, 3 with bipolar disorders, 3 with major depressions, and 3 with organic diagnoses. There was no significant difference in BIS scores between different diagnoses (analysis of variance, $p = .914$) even for post hoc tests.

Table 1. Comparison of Participants Who Did and Did Not Complete the Social Functioning Scale at 18 Months

Characteristic	Completers (N = 158)	Noncompleters (N = 99)
Sex, male, %	68	70
Ethnicity, %		
White	92	81
African/Caribbean	6	10
Other	3	9
Diagnosis, %		
Schizophreniform disorder	38	42
Schizophrenia	32	39
Schizoaffective disorder	14	10
Delusional disorder	10	5
Psychosis not otherwise specified	6	3
Substance dependence, %	16	16
Age at onset, median (IQR), y	27 (22–33)	26 (21–33)
Education, median (IQR), y	11 (10–13)	11 (10–13)
DUP, median (IQR), wk	10 (5–28)	12 (5–40)
Baseline PANSS, mean (SD)	88 (16)	89 (18)
Baseline SFS, mean (SD)	114 (34)	125 (32)
Baseline BIS, mean (SD)	9.8 (4.1)	8.9 (4.3)

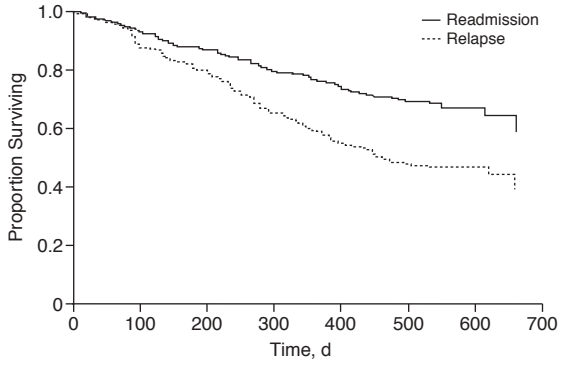
Abbreviations: BIS = Birchwood Insight Scale, DUP = duration of untreated psychosis, IQR = interquartile range, PANSS = Positive and Negative Syndrome Scale, SFS = Social Functioning Scale.

Relapse and Readmission

Data on relapse over 18 months were available for 92% (N = 236), of whom 51% (N = 120) met relapse criteria (Figure 1). All cases had data on readmission: 84 (33%) were readmitted during follow-up.

Insight at baseline was significantly lower in those who relapsed (BIS mean = 8.8) than those who did not (mean = 10.3; 95% CI for the difference = 0.32 to 2.66; $p = .013$). It was lower in those rehospitalized (mean = 8.1) than in those who were not (mean = 10.2; 95% CI for the difference = 0.84 to 3.40; $p = .001$). There was no statistically significant association between having missing baseline BIS data and the occurrence of relapse or of readmission (Fisher exact test, $p = .262$ and $p = .878$, respectively) or between having missing baseline SFS data and the occurrence of relapse or of readmission (Fisher exact test, $p = .082$ and $p = .879$, respectively). Multiple logistic regression showed that the only potential confounder in our list to be associated with missing BIS score or SFS score outcomes is treatment center. That is, the baseline BIS and SFS data are missing completely at random within each of the treatment centers. The following stratified survival analyses are based on the participants with complete data and would therefore appear to be statistically valid, if not necessarily optimally efficient.

Figure 1. Proportion of the Sample Surviving Without Readmission or Relapse During Follow-Up (N = 236)



The BIS score predicted relapse after simultaneous adjustment for the confounders listed above (estimated hazard ratio, 0.943; 95% CI = 0.892 to 0.996; p = .035). Those with the poorest insight have a BIS score of 0; the best have a score of 16. Each additional point on the BIS scale multiplied the hazard by 94.3%. An increase in, for example, 3 points therefore decreased the hazard by 0.943 × 0.943 × 0.943 or 83.8%. The estimated rate of relapse for those with the best insight scores was therefore 39% of that of those with the worst (zero) scores (95% CI = 16% to 93%). Poor insight also predicted readmission (hazard ratio, 0.934; 95% CI = 0.876 to 0.996; p = .036); readmission was highly correlated with relapse. Therefore, for readmission, the hazard ratio for those with maximum insight (scoring 16) was 34% (95% CI = 12% to 93%) of the hazard ratio of those scoring 0.

Attitudes toward medication (DAI score) did not differ significantly between those who did and did not relapse and who were and were not readmitted. The BIS has 3 subscales measuring awareness of the need for treatment, awareness of psychiatric illness, and the ability to relabel symptoms as psychotic.[35] Post hoc, the BIS total was replaced with each of the subscales in turn in the Cox regressions predicting relapse and readmission. Only "relabeling symptoms" was a significant predictor of relapse (estimated hazard ratio, 0.841; 95% CI = 0.712 to 0.994) and readmission (hazard ratio, 0.777; 95% CI = 0.635 to 0.950).

PANSS and SFS Outcome

The Pearson correlation of baseline BIS total with final PANSS total was –0.172 (95% CI = –0.322 to –0.013; p = .034), but baseline BIS and final SFS did not correlate significantly. First, these unadjusted associations were checked by fitting a bivariate linear regression model in Mplus (one equation for 18-month PANSS total and one for 18-month SFS total) with none of the potential confounders in the regression equations for the 2 outcomes. The results from fitting this model confirmed the results using correlations. The estimated regression coefficient for the effect of BIS total score on 18-month PANSS total score was –0.813 (95% CI = –1.513 to –0.113) and for the effect of BIS total on 18-month SFS score was 0.161 (95% CI = –1.242 to 1.564). We then fitted the full model with all potential confounders included in addition to the effects of baseline BIS in both regression equations. The estimated regression coefficients for the effect of BIS total score on 18-month PANSS total score in this model was now –0.363 (95% CI = –0.931 to 0.205), that is, no longer statistically significant. The estimated regression coefficient for the effect of BIS total score on 18-month SFS total score in this model was 0.699 (95% CI = –0.628 to 2.026), again in the expected direction but not significant.

Simultaneously constraining the 2 effects of BIS in the bivariate regression model to be zero provides a global test of the effect of BIS on PANSS and SFS. The difference in the log likelihoods for the unconstrained and constrained models provided a χ^2 of 1.80 (df = 2, p > .2). That is, without confounders the fit of a model where BIS was constrained to have no association with PANSS or SFS was not significantly worse than the model where BIS varied freely.

DISCUSSION

Strengths

This was a medium-term, prospective follow-up of a geographically defined cohort of cases with first-episode schizophrenia and related psychoses. A high proportion of patients consented to participate and the randomized treatment involved did not affect relapse, readmission, or insight significantly.[31,32] Seventy-two percent were reinterviewed, and relapse and readmission data were available on almost the whole cohort. Analyses suggested little bias due to dropout. The sample was large enough to detect correlations of under 0.20 with at least 80% power. It was the first such study to include a detailed measure of insight.

Limitations

Limitations include that this was a study of first admission to inpatient and day-patient units, not first contact. However, in the United Kingdom, even in services with highly developed community treatment, 80% of patients are eventually admitted as inpatients.[43] Relapse was assessed by casenote review, whereas it is best assessed by repeated longitudinal observations. The measure of substance abuse was simple and only applied at baseline.

In What Way Does Insight Predict Outcome?

Poor awareness on the BIS was a predictor of early relapse and consequent readmission. There were consider-

able differences in vulnerability between those at opposite ends of the insight spectrum. Insight had no significant effect on the SFS or the PANSS at final interview. Thus poor insight promoted relapse but did not lead to persistent, significant worsening of symptoms or disability. Poor insight at presentation can be added to the list of prognostic variables for the important early phase of schizophrenia. Whether recognizing this association leads to a useful intervention depends on why it occurs.

The subscale of the BIS most related to outcome was that measuring relabeling symptoms. There was no evidence that awareness of illness or acceptance of treatment were predictive, just as attitudes toward medication measured at 6 weeks by the DAI appeared unrelated to relapse. However, this analysis of BIS subscales was post hoc.

On the face of it these findings imply that insight's effect on outcome is via processes unrelated to adherence, for example, continued substance misuse. Those with better insight could also seek help and reduce stress earlier in relapse, though to avoid meeting full criteria participants would have to avert deterioration sufficient to change management within 2 weeks. Yet emerging findings[21–24] about the complexity of first-episode schizophrenia patients' attitudes and medication use leave open the possibility that adherence plays a role. Postulating adherence as a mediator is attractive since it is such a powerful predictor of first relapse[13] (and plausibly readmission) without other poor outcomes, which explains our findings and those of Van Os et al.[14]

Kampman et al.[21] found both insight into symptoms and negative attitudes toward medication were associated with 59 patients' prediction of poor adherence, though not with initial compliance (90% were hospitalized). However, their sample was small compared to the number of variables in their logistic regression models. Mutsatsa et al.[22] found that global insight, as well as attitudes toward treatment, predicted adherence soon after first admission. Perkins' group[24] found that what predicted adherence was recognition of the recent benefits of medication (and need for treatment) but not simple negativity about medication, compliance to external encouragement, or perceived side effects. The Perkins et al. sample was selected by entry into a trial; moreover, recognizing symptoms was not included in their analysis, which was based on a health beliefs model.

One synthesis of these results is that what predicts sustained adherence is recognition of symptoms and their amelioration by medication, leading to valuing medications' future benefits. If so, assessing patients' recognition of symptoms and their attitudes toward the recent and potential future benefits of medication are useful ways to predict adherence, relapse, and readmission. Similar evaluations of symptoms and illicit drugs' effects might reduce their use. More research into the details of these relationships in this unique group could permit improved interventions focused on these attitudes.

CONCLUSIONS

Insight is a construct of disputed phenomenological status but undoubted clinical importance in schizophrenia. In first-episode nonaffective psychosis, poor initial insight predicted relapse and readmission but neither symptoms nor social function at follow-up. Poor recognition of symptoms was the aspect of initial insight that best related to outcome. There was no strong evidence concerning what secondary variable mediated insight's effects—broad attitudes toward medication did not appear to do so. A more sophisticated view of what assumptions and beliefs in the earliest stages of psychosis produce behaviors that later promote relapse could inform successful intervention.

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Appendix 1. Birchwood Insight Scale[a]

Each item is scored:
0: no insight (Yes to 2, 3, 6 and 8; No to the others)
1: unsure (all items)
2: insight (No to 2, 3, 6 and 8; Yes to the others)

	Yes	*Unsure*	*No*
1. Some of my symptoms are made by my mind.	❑	❑	❑
2. I am mentally well.	❑	❑	❑
3. I do not need medication.	❑	❑	❑
4. My stay in hospital is necessary.	❑	❑	❑
5. The doctor is right in prescribing medication for me.	❑	❑	❑
6. I do not need to be seen by a doctor or psychiatrist.	❑	❑	❑
7. If someone said I have a nervous or a mental illness then they would be right.	❑	❑	❑
8. None of the unusual things I experience are due to an illness.	❑	❑	❑

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