

Prediction of Outcome Following a First Episode of Schizophrenia A Follow-up Study of Northwick Park First Episode Study Subjects

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Background. Although previous studies have attempted to identify predictors of outcome in schizophrenia, few have prospectively studied first episode patients for an adequate follow-up period.

Method. The psychopathological predictors of outcome were investigated in a subgroup of 51 subjects, originally included in the Northwick Park study of first episode schizophrenia who were followed up 7.3 years (s.d. 1.1, range 5.3–10.3) after first admission in the Harrow study. Forty-four subjects (24 men, 20 women) were traced. Outcome measures were time to first readmission, occupational level and total duration of hospital admission at five years after first admission.

Results. A survival analysis of time to first relapse revealed that the presence of subjective feelings of depression (CATEGO syndrome SD) during the first admission was associated with early relapse while the presence of depressive delusions (CATEGO syndrome DD) and higher educational attainment protected against early relapse. Total duration of hospitalisation at five years after first onset was positively associated with the presence of CATEGO syndromes SD and OD (biological features of depression) and negatively associated with female sex. Poor occupational outcome was not significantly associated with any psychopathological predictors.

Conclusions. Our findings challenge the conventional view that symptoms of depression are associated with better outcome in schizophrenia.

Many studies have attempted to find predictors of outcome in schizophrenia (McGlashan, 1988). Most of these have been retrospective or have included subjects at a variety of stages in the course of the illness. It is unusual to have the opportunity of conducting a prospective follow-up investigation of more than five years duration from the time of the first episode of the illness, especially in patients who were not selected by their compliance with clinical trial protocols. Our study aimed to identify the predictors of outcome in a group of subjects who had been included in the Northwick Park study of first episodes of schizophrenia (Johnstone *et al*, 1986) and who subsequently fell within the remit of the Harrow study of the disabilities and circumstances of schizophrenic patients (Johnstone, 1991).

Method

Subjects

The subjects were identified by linking the two previous studies. The Northwick Park study of first episodes of schizophrenia (FES; Johnstone *et al*, 1986) was a multicentre study of 253 patients who were first admitted with a diagnosis of schizophrenia to one of nine medical centres in London between

August 1979 and December 1981. The inclusion criteria are shown in the Appendix. The study examined presentation of illness, short-term outcome, and the role of expressed emotion in relapse; a subgroup of 120 of the sample were entered in a two year, randomised, placebo-controlled trial of prophylactic neuroleptic medication.

The second study was the Harrow study of the disabilities and circumstances of schizophrenic patients (Johnstone, 1991). In this study, attempts were made (between 1 February 1987 and 1 January 1990) to trace all patients fulfilling St Louis criteria (Feighner *et al*, 1972) for definite or possible schizophrenia ($n = 532$) who were discharged from Harrow beds (Northwick Park and Shenley Hospitals) between 1 January 1975 and 1 January 1985.

Although Northwick Park Hospital had national beds and therefore did not serve a strictly catchment area population, the FES involved nine medical centres within a 35-mile range of Northwick Park Hospital. The researchers were notified of all potentially suitable admissions to those hospitals. Any subject resident in Harrow at the time of developing an illness who was admitted to these other hospitals would therefore have been identified. There were none. Subjects treated entirely within non-NHS

services would not have been detected, but local experience suggests that this is rare. Thus we can be reasonably sure that the FES included all cases of first-episode schizophrenia occurring in Harrow during the period August 1979–December 1981, together with some patients from adjacent boroughs.

Predictor variables

Because of the small sample size, we were selective about the number of potential predictor variables examined in the present study. It is rare to have standardised psychopathological data from the time of the first episode, especially in combination with a reasonably long follow-up period. Earlier work has found certain features of mental state to be associated with good prognosis, in particular, the presence of depressive features, anxiety, confusion or perplexity, concern with death and subjective distress and the absence of thought disorder (McGlashan, 1988).

In the FES study, all patients were assessed using the Present State Examination (PSE; Wing *et al.*, 1974) at entry. We chose to investigate the effect on outcome of the psychopathological items measured by the PSE. The CATEGO computer program organises the 140 symptoms assessed by the PSE into 35 syndromes. We used the following syndromes as potential predictor variables:

- (a) SD (Simple depression, consisting of symptoms 19 Inefficient thinking, 23 Depressed mood, 24 Hopelessness, 25 Suicidal plans or acts, 121 Depression on examination)
- (b) ED (Special features of depression, consisting of symptoms 29 Self-depreciation, 32 Guilty ideas of reference, 33 Guilt, 51 Dulled perception, 54 Dulled affect)
- (c) OD (Other symptoms of depression, consisting of symptoms 27 Morning depression, 34 Loss of appetite, 37 Early wakening, 38 Loss of libido, 39 Premenstrual exacerbation)
- (d) DD (Depressive delusions and hallucinations, consisting of the symptoms 61 Depressive hallucinations, 88 Delusions of guilt, 91 Hypochondriacal delusions, 92 Delusions of catastrophe)
- (e) GA (General anxiety, consisting of the symptoms 11 Anxiety, 14 Panic attacks, 120 Anxiety on examination)

and also the PSE symptoms:

1. Symptom 102 (clouding or stupor)
2. Symptom 126 (perplexity)
3. Symptom 128 (blunted affect).

Each of these psychopathological items was coded as a dichotomous variable (0 = absent, 1 = present). Several other baseline variables which have previously been shown to have prognostic power were investigated: duration of illness preceding first admission, age at first admission, sex, educational attainment (dichotomised into A-levels or equivalent or above: 0 = no, 1 = yes).

Outcome variables

Outcome was evaluated in three ways:

(a) Time to first readmission following discharge after the first episode. This survival function was investigated using a proportional hazards regression model. Univariate hazard ratios (HR) were calculated for each predictor variable and those significantly associated with outcome were then entered into a stepwise regression model. The model produced was then extended by the remaining variables to determine whether they significantly improved the model.

(b) Aggregated duration of hospital stay at five years after first admission. A stepwise multiple regression analysis was performed to determine which independent variables best predicted length of stay, which was logarithmically transformed for the analysis.

(c) Occupational level as classified in terms of the Office of Population Censuses and Surveys *Classification of Occupations* (1980) at five years after first admission. The sample was dichotomised into two groups (i) 'good' outcome (occupation better or the same as at first admission) and (ii) 'poor' outcome (unemployed or a poorer level of occupation). Logistic regression analysis was performed to identify any predictor variables associated with occupational outcome at five years.

Results

Sample characteristics

Fifty-one of the subjects in the FES were discharged from Harrow hospitals and met St Louis criteria for schizophrenia, making them eligible for inclusion in the Harrow study. Of these, 44 (86%) patients were traced. Two males had died from unnatural causes. Twenty-six (59%) of the subjects were resident within the catchment area of Northwick Park Hospital at the time of first admission, 10 (23%) were from surrounding London boroughs within a 10-mile radius of the hospital, 7 (16%) were from further afield and 1 (2%) was of no fixed abode. All the surviving subjects (22 men and 20 women) received comprehensive, standardised assessments. The mean age at first onset was 27.3

years (s.d. 9.4, range 16–56) and the mean age at first admission was 28.4 years (s.d. 9.8, range 17–57). Males tended to be younger, although this was not statistically significant in this small sample. The mean duration of follow-up of the surviving 42 subjects was 7.3 years (s.d. 1.1, range 5.3–10.3).

After five years, 24% (10) of the surviving subjects had not been readmitted to hospital, 21% (9) had had one further admission, 21% (9) two, 12% (5) three and 23% (10) had been admitted on four or more occasions. By the end of follow-up, 8 (19%) subjects had not been readmitted. This group is unusual and their clinical features are summarised in Table 1. All these subjects were classified as S+ by CATEGO, indicating the presence of at least one Schneiderian first rank symptom.

Time to first readmission

The eight subjects who were not readmitted during the observation period were treated as censored observations. Nine per cent of the subjects were readmitted within one month of discharge, 34% within six months, 36% within one year, 55% within two years and 80% within five years.

Three predictor variables (presence of CATEGO syndromes SD and DD, education to A-level standard or above) were associated with risk of admission in the univariate proportional hazard analysis. These three variables were entered into a multivariate model which was extended by each of

the remaining variables in turn and a score test performed. No further variables were significant additions to the model. The presence of CATEGO syndrome SD was associated with a higher risk of readmission (adjusted hazard ratio (HR) 3.90, 95% CI 1.62–9.39, $P=0.002$). Education to A-level standard or above (HR 0.20, 95% CI 0.08–0.52, $P<0.001$) and the presence of CATEGO syndrome DD (HR 0.27, 95% CI 0.13–0.60, $P=0.001$) were associated with a decreased risk of admission. Overall, the likelihood ratio statistic for this model was 27.25 on 3 d.f. ($P<0.001$).

Outcome according to aggregated duration of hospital admission

In the multiple regression model, the presence of CATEGO syndromes SD (coefficient 0.335, 95% CI 0.154–0.515, $P=0.0006$) and OD (coefficient 0.068, 95% CI 0.008–0.129, $P=0.03$) were positively associated with total duration of hospital admission at five years. Female sex was associated with a shorter total duration (coefficient -0.168 , 95% CI -0.335 to -0.001 , $P=0.05$). This regression model explained approximately 42% of the variance in the total duration of hospital admission in the sample.

Outcome according to occupation

None of the baseline variables were significantly associated with occupational outcome at five years.

Table 1
Clinical features of subjects who were not readmitted by the end of the follow-up period

Age at onset	Sex	Summary
44	F	Premorbid social isolation. On admission described auditory hallucinations which she attributed to the Devil. Believed that the Yorkshire Ripper intended to kill her. Odd attire. Positive symptoms responded to neuroleptics. At follow-up, function uncertain because of financial independence
25	F	On admission, perplexed with many misperceptions. Described thought interference, fragmentary hallucinations and religious delusions. Responded quickly to treatment and functioning well as administrator at follow-up
57	F	Long history of sexual delusions, somatic hallucinations and somatic passivity before first admission. Responded well to treatment although suffered severe movement disorder and experienced minor deterioration when drugs reduced. Good function at follow-up
37	F	Partially deaf, describing incessant auditory hallucinations and paranoid delusions concerning the BBC and a religious network. Very supportive husband and fairly well on treatment at follow-up
23	M	At first assessment, described auditory hallucinations, thought echo and paranoid delusions. Incongruous affect. His flat was covered with string. Never engaged with services and probably constantly psychotic
23	M	Sudden onset of delusions, thought broadcast and auditory hallucinations. Remitted gradually with treatment over several months. Subsequently occupationally very successful with occasional minor recurrence of symptoms. Drugs reduced and finally stopped.
34	M	Acute onset with gross formal thought disorder, perplexity, hallucinations, thought insertion/withdrawal, paranoid delusions and passivity feelings. After several months symptoms remitted and subsequently worked as a teacher, maintained on neuroleptics. Socially restricted compared with premorbid function
20	F	Described thought alienation and auditory hallucinations on first admission. Six-month history of bizarre behaviour. Symptoms remitted quickly. Denied illicit drug ingestion at admission but at follow-up admitted to heavy and prolonged use

Discussion

This study found that subjective feelings of depression and hopelessness (CATEGO syndrome SD) at the time of first admission with schizophrenia predicted earlier first readmission. Higher educational level and the presence of depressive delusions (CATEGO syndrome DD) were protective against first readmission. The presence of CATEGO syndromes SD and OD (biological features of depression) was associated with a longer duration of hospital admission at five years. Women had a shorter total duration of admission. Occupational outcome was not associated with any of the baseline characteristics studied.

The study has several limitations. The small sample size reduces its power and precision. The sample was not drawn from a strict catchment area. Furthermore, the outcome measures used do not necessarily accurately reflect global outcome. However, the World Health Organization Determinants of Outcome Study found duration of hospitalisation to be highly associated with global outcome at two years in patients in developed countries (Jablensky *et al*, 1992). It was not significantly associated with occupational outcome in the present study. However, despite these limitations, the study also has methodological strengths. Most importantly, the standardised assessment of mental state, blind to the eventual outcome, was performed in a sample of first episode schizophrenic patients.

The finding that female gender and higher educational attainment were associated with more favourable prognosis is consistent with previous studies (McGlashan, 1988). The most intriguing finding is that, contrary to conventional views, subjective feelings of depression on first admission are associated with a poor outcome measured in terms of earlier readmission to hospital and longer total duration of hospital admission. This is an unexpected finding in view of the long-held belief that affective symptoms are associated with good prognosis (McGlashan, 1988). However, several previous studies have found that depressive symptoms do not predict outcome or are associated with poor outcome at two years (Gift *et al*, 1980). Shepherd *et al* (1989) described a correlation between number of readmissions and depressive episodes during follow-up, supporting their previous finding that patients with a primary diagnosis of schizophrenia are frequently admitted to hospital with depressive symptoms independent of exacerbations of florid schizophrenia. Depressive symptoms are common in both acute schizophrenic episodes (Jablensky *et al*, 1992) and during the course of the disorder and are probably

associated with positive symptoms of schizophrenia (Barnes *et al*, 1989), often improving as the psychotic symptoms subside with treatment (Knights & Hirsch, 1981).

Previous studies reporting that depressive symptoms predict good prognosis suffered from methodological flaws including inappropriate sampling, unsystematic collection of symptom data (often retrospective and failing to detect depression) and unreliable diagnostic methods (Gift *et al*, 1980). It is noteworthy that in the present study the presence of depressive delusions (CATEGO syndrome DD), which may be more likely to be detected in retrospective case note studies, protected against early relapse.

Appendix

Inclusion criteria for Northwick Park study of first episodes of schizophrenia

1. Age 15–70 years.
2. Presence of first psychotic episode, defined as: (a) no past diagnosis of psychosis or possible psychosis, (b) no previous in-patient care exceeding three days (excluding (i) out-patient care leading to this first admission and where there was no lapse of care exceeding 30 days, (ii) medication with neuroleptic-containing preparations advocated for use in non-psychotic conditions).
3. Admission to in-patient or day patient care for at least one week.
4. A clinical diagnosis of schizophrenia made by the referring clinician.
5. Categories S, O or P on PSE.
6. Absence of organic disease with definite or probable aetiological significance.

References

- BARNES, T. R. E., CURSON, D. A., LIDDLE, P. F., *et al* (1989) The nature and prevalence of depression in chronic schizophrenic in-patients. *British Journal of Psychiatry*, **154**, 486–491.
- FEIGNER, J. P., ROBINS, E., GUZE, S. B., *et al* (1972) Diagnostic criteria for use in psychiatric research. *Archives of General Psychiatry*, **26**, 57–63.
- GIFT, T. E., STRAUSS, J. S., KOKES, R. F., *et al* (1980) Schizophrenia: affect and outcome. *American Journal of Psychiatry*, **137**, 580–585.
- JABLENSKY, A., SARTORIUS, N., ERNBERG, G., *et al* (1992) Schizophrenia: manifestations, incidence and course in different cultures. *Psychological Medicine Monograph Supplement*, **20**, 1–97.
- JOHNSTONE, E. C. (ed.) (1991) Disabilities and circumstances of schizophrenic patients – a follow-up study. *British Journal of Psychiatry*, **159** (suppl. 13).
- , CROW, T. J., JOHNSON, A. L., *et al* (1986) The Northwick Park study of first episodes of schizophrenia 1. Presentation of the illness and problems relating to admission. *British Journal of Psychiatry*, **148**, 115–120.
- KNIGHTS, A. & HIRSCH, S. R. (1981) “Revealed” depression in schizophrenia. *Archives of General Psychiatry*, **38**, 806–811.

- McGLASHAN, T. (1988) A selective review of recent North American long-term follow-up studies of schizophrenia. *Schizophrenia Bulletin*, 14, 515.
- OFFICE OF POPULATION CENSUSES AND SURVEYS (1980) *Classification of Occupations*. London: HMSO.
- SHEPHERD, M., WATT, D., FALLOON, I., *et al* (1989) The natural history of schizophrenia: a five year follow-up study of outcome and prediction in a representative sample of schizophrenics. *Psychological Medicine*, Monograph suppl. 15, 1-46.
- WING, J. K., COOPER, J. E. & SARTORIUS, N. (1974) *The Measurement and Classification of Psychiatric Symptoms*. Cambridge: Cambridge University Press.

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