

Natural course of schizophrenia: 2-year follow-up study in a rural Chinese community[†]

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Background A number of studies have questioned whether the natural course of schizophrenia is more favourable in 'developing' than 'developed' societies and whether culture is a factor in producing a favourable course.

Aims This prospective study tests the hypothesis that the natural outcome of schizophrenia would be favourable in a Chinese rural area.

Method We investigated all patients with schizophrenia, including patients who had not received any treatment, among 149 231 rural community population in Xinjin County, Sichuan in 1994. Those patients who had never received treatment were followed up for two years.

Results Three-quarters of patients with schizophrenia who had not been treated remained symptomatic. As the duration of illness increased, the illness became more serious. The clinical outcome of the drug-treatment group was significantly better than for patients who had not received any treatment.

Conclusions The natural clinical outcome of schizophrenia in the Chinese rural community was poor, and occupational functioning of patients with schizophrenia was comparatively better. Schizophrenia itself has a specific natural course – antipsychotic drug treatment and psychosocial treatment will produce an improvement in prognosis.

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Many studies have revealed that the course of schizophrenia is more favourable in 'developing' than 'developed' societies (Sartorius *et al*, 1977; Waxler, 1979). Anti-psychotic drug treatment can dramatically improve the prognosis of patients with schizophrenia, and relapse rates are much lower in patients given maintenance treatment with antipsychotic medication (Leff *et al*, 1991). Gender effects among patients with schizophrenia have frequently been reported in the course of illness and outcome (Salokangas, 1983). But there are only a few studies about the natural course of schizophrenia 'unaffected' by anti-psychotic drug treatment.

In contrast, other investigators reported that the evidence for a more favourable course in developing societies was not conclusive. Indeed, a favourable course has also been reported in various industrialised societies (Edgerton & Cohen, 1994). In order to identify the natural course of the illness and factors affecting it, we identified a prevalence sample of patients with schizophrenia from Xinjin County, Sichuan province and followed up those who had never received any treatment from March 1994 to April 1996.

METHOD

Study subjects

The total population in the rural area of Xinjin County (framework populations) was 235 546. The six townships (including 149 231 people in the rural community) were randomly selected from all 14 townships of Xinjin County in the south of Chengdu. An epidemiological investigation of all members of rural communities was conducted in the six townships of Xinjin County in March 1994. Methods used were the same as those reported by Shen *et al* (1986) and Cooper & Sartorius (1996) in

a 1982 survey. We carried out face-to-face interviews with the head of each household (together with the key informant method) in order to identify potential cases of severe mental disorder. The Screening Schedule for Psychoses (Shen & Wang, 1985) was completed via interview with the head of the household, and discussion with village doctors and neighbours comprising the survey sample. All the patients who met the schizophrenia criteria of the Chinese Classification and Diagnostic Criteria of Mental Disorder (CCMD-2-R) (Yang, 1989) and the ICD-10 (World Health Organization, 1982) were included in the study. Then all patients with schizophrenia were followed up for 2 years.

Measurement

Widely used national epidemiological schedules and rating scales were used to assess symptoms and social abilities. Standard instruments including the Screening Schedule for Psychoses, Present State Examination (PSE-9, Chinese translation), the General Psychiatric Interview Schedule and Summary Form (including the project diagnosis), and the Social Disability Screening Schedule (SDSS) were used (Shen & Wang, 1985; Shen *et al*, 1986; Cooper & Sartorius, 1996). When positive answers were obtained for a subject on the screening procedures for psychosis, a comprehensive general psychiatric interview was then completed with that subject by an investigator who was a member of the survey team. All the investigators were lecturers, associate professors and professors of psychiatry. The senior professor trained investigators, reviewed all ratings and completed ratings for many of the patients. The mean percentage agreement on the Screening Schedule for Psychoses, PSE-9 and SDSS on the ratings for 10 patients ranged from 80.5 to 99.0%. Kappa values between pairs of investigators ranged from 0.74 to 1.0. Two main assessments were conducted, the first at the beginning of the study, and the second at the end of the follow-up period.

RESULTS

Number of cases identified and prevalence rates

Of the 123 572 people aged 15 years and over assessed using the Screening Schedule for Psychoses, a total of 510 were identified as either having schizophrenia at the time

[†]See invited commentary, p. 159, this issue.

of the survey ($n=367$), or as having recovered but had a history of schizophrenia in their past ($n=143$). This gives a point prevalence rate of 2.97 per 1000 population aged 15 years and over, and a total prevalence rate of 4.13 per 1000.

Treatment and management

Thirty of the 510 patients (5.9%) maintained regular antipsychotic treatment (regular treatment group) for more than one year, and 156 (30.6%) received no treatment at all (never-treated group). The others were treated by a variety of agencies, including: trained practitioners of traditional Chinese medicine (such as acupuncture and herbal remedies – traditional treatment group), psychiatric hospitals, psychiatric out-patient clinics, and local healers, but received irregular treatment or discontinued treatment (brief and/or irregular treatment group), as shown in Table 1.

All the 510 patients were in the age range 15–95 years; the mean age, age of onset and duration of illness for the four groups of patients are shown in Table 2.

The results indicated that the duration of illness in the regular treatment group was significantly shorter than that in the brief and/or irregular treatment, traditional treatment and never-treated groups.

Characteristics of patients who had never received treatment

Of the total 156 patients who had never been treated at all, 39.7% were single, 41.7% were married, 8.3% were divorced, and 10.3% were widows or widowers. This divorce rate is very much higher than that of the overall Chinese sample in the Nationwide Epidemiological Survey, 1982 ($<1\%$) (Cooper & Sartorius, 1996). The gender ratio (male:female) was 1:0.93, and no significant difference was found between the proportion of males ($n=81$, 51.9%) and females ($n=75$, 48.1%; $P>0.05$). The marital status indicated that the sample included more unmarried male patients (42.0%) than female patients (4.0%; $P<0.01$); the mean (s.d.) number of people per household was 3.45 (1.50), and 34 patients (21.8%) lived alone. The rate of illiteracy or those who had never attended school was 25.0%, 57.1% had attended primary school and 17.9% had attended middle school. The socio-economic level of each household was assessed: 5.8% were high, 32.0% were middle and 62.2% were low. This indicated that most patients who had never received treatment were from a poorer family background.

The reasons for not receiving treatment included: lack of money ($n=55$, 35.3%); relatives' uncertainty about the patients' illness (or not thinking the patient was suffering from mental illness) ($n=46$, 29.5%);

patients' refusing to accept drug treatment ($n=29$, 18.6%); no relatives to care for patient ($n=23$, 14.7%); and local unavailability of medical facilities ($n=3$, 1.9%).

The 10 most frequent symptoms of schizophrenia in 156 patients (PSE-9 definitions) were: delusions of persecution (39.7%), apathy (34.0%), incongruity of affect (28.2%), splitting of thought (26.3%), withdrawal (24.4%), affectively neutral auditory hallucinations (21.2%), delusion of observation (21.2%), auditory hallucinations (commentary) (19.2%), poverty of thought (17.9%), and other delusions (15.4%).

Patients' ability to work

Among the patients who had never received treatment, the percentages of patients who could do full- or part-time farm- or housework, or could do no work were 32.1% ($n=50$), 45.5% ($n=71$) and 22.4% ($n=35$), respectively.

Social disability

Among the patients with schizophrenia who had never received treatment, there were 129 (82.7%) whose social ability was rated as being more than a mild disability. Of the 129 patients, 69 (53.5%) were rated as having the most seriously impaired social functioning, 19 (14.7%) were rated as serious, 14 cases (10.9%) were rated moderately impaired, and 27 cases (20.9%) were rated as mildly impaired.

Suicidal thoughts and behaviour

Of the 156 patients who had not received treatment, seven had experienced suicidal thoughts or behaviour during their illness history. The rate of suicidal thought and behaviour was 4.5%. The prevalence of suicidal thoughts and behaviour found in this study was not consistent with some previously published reports in Western countries (Black *et al*, 1985; Landmark *et al*, 1987). Between 20% and 42% of patients with schizophrenia attempt suicide, and 10–15% are successful in these studies. The results of our study were the same as that found in a study in India (Verghese *et al*, 1989). This might be caused by cultural differences and differences in the groups of patients studied. In a rural area of China, the patients with schizophrenia might endure less social

Table 1 Treatment received by 510 patients with schizophrenia

Treatment	<i>n</i> (%)
Maintained regular antipsychotic treatment for more than one year (regular treatment group)	30 (5.9)
Hospitalised once or maintained irregular or discontinued antipsychotic treatment (brief and/or irregular treatment group)	218 (42.7)
Traditional Chinese method (traditional treatment group)	106 (20.8)
No treatment (never-treated group)	156 (30.6)

Table 2 Patients' age, age of onset and duration of illness

	Regular treatment group ($n=30$)	Brief and/or irregular treatment group ($n=218$)	Traditional treatment group ($n=106$)	Never-treated group ($n=156$)	<i>P</i>
Mean age (s.d.)	35.9 (13.4)	42.3 (14.5)	47.3 (16.8)	48.2 (15.2)	>0.05
Age of onset (s.d.)	27.9 (10.0)	28.9 (12.0)	32.3 (13.8)	34.2 (13.4)	>0.05
Duration (years)	7.8 (7.5) ^a	12.7 (10.4) ^b	15.0 (11.6) ^c	13.6 (12.1) ^d	

ab $F=5.546$, $P=0.019$; ac $F=9.974$, $P=0.002$; ad $F=11.193$, $P=0.001$; bc $F=2.819$, $P=0.094$; cd $F=0.182$, $P=0.670$.

Table 3 Clinical status among the four groups

	Cases	Complete remission (%)	Partial remission (%)	Marked symptoms (%)	Deteriorated (%)
Regular treatment ^a	30	30.0	36.7	26.7	6.6
Brief and/or irregular treatment ^b	218	31.2	14.2	45.9	8.7
Traditional treatment ^c	106	31.1	13.2	44.4	11.3
No treatment ^d	156	9.6	8.3	75.7	6.4
Total	510	24.5	13.4	53.7	8.4

ab $\chi^2=10.222$, d.f.=3, $P=0.016$; ac $\chi^2=9.172$, d.f.=3, $P=0.027$; bc $\chi^2=0.673$, d.f.=3, $P=0.880$; bd $\chi^2=39.372$, d.f.=3, $P<0.001$; cd $\chi^2=33.329$, d.f.=3, $P<0.001$.

pressure and discrimination than in other places.

Baseline clinical status

The baseline clinical status of the 510 patients with schizophrenia is shown in Table 3. The clinical status in the regular treatment group was significantly better than that in the brief and/or irregular treatment, traditional treatment, and never-treated

groups ($P<0.05$). No significant difference was found between the brief and/or irregular treatment and traditional treatment groups in clinical status. This result might be caused by the fact that none of the patients maintained regular drug treatment in the brief and/or irregular treatment group. Meanwhile, this result also supports the theory that the Chinese traditional treatment group will have a slightly improved outcome. The clinical status of the never-

treated group was the worst of the four groups ($P<0.001$).

Factors affecting outcome

For the 156 patients with schizophrenia who had never received treatment, the study showed that patients' mean age, age of first onset, family history of mental illness, marital status, psychosocial factors and their family care state were not significantly

Table 4 Factors affecting clinical outcome of never-treated patients

Factor	Cases <i>n</i>	Complete remission (%)	Partial remission (%)	Marked symptoms (%)	Deterioration of illness (%)	<i>P</i>
Gender						
Male	81	3.70	6.17	80.25	9.88	< 0.05
Female	75	16.00	10.67	70.67	2.66	
Age (years)						
< 40	40	7.50	12.50	70.00	10.00	> 0.05
≥ 40	116	10.34	6.90	77.59	5.17	
Age of first onset (years)						
< 40	106	8.49	9.43	73.59	8.49	> 0.05
≥ 40	50	12.00	6.00	80.00	2.00	
Duration of illness (years)						
< 1	14	35.72	7.14	57.14	0	< 0.05
1–5	37	5.40	8.11	78.38	8.11	
≥ 5	105	7.62	8.57	77.14	6.67	
Family history of mental illness						
Yes	53	11.32	3.78	75.47	9.43	> 0.05
No	103	8.74	10.68	75.73	4.85	
Marital status						
Partner	65	6.15	3.08	83.08	7.69	> 0.05
No partner	91	12.09	12.09	70.33	5.49	
Family care state						
Good	97	12.37	9.28	72.16	6.19	> 0.05
Insufficient	59	5.08	6.78	81.36	6.78	
Psychosocial factors						
Yes	51	17.65	5.88	72.55	3.92	> 0.05
No	105	5.72	9.52	77.14	7.62	

related to the clinical outcome ($P > 0.05$) (see Table 4). There were 58.3% patients who had no partner or had not married, and 37.8% of patients whose family care status was poor. All these results showed that their social support state was not good.

There was a significant difference in the natural clinical outcome between male and female patients ($P < 0.05$). The female patients' clinical prognosis and rate of complete remission were better and higher than those of male patients. More male patients had marked symptoms and deteriorated.

Among those patients whose duration of illness was less than 1 year, there were five cases (35.7%) who recovered fully, and none deteriorated. For those patients whose duration of illness was more than 1 year, the percentage of complete remission was less than 7.6%, and deterioration more than 6.7%. The results strongly indicate that the longer the duration of the illness, the worse the patient's prognosis ($P < 0.05$).

Outcome at follow-up

We followed up all the patients who had never received treatment for 2 years. We provided community mental health services in the pilot area, during the follow-up period, and 55 people (35.3%) accepted treatment. Six patients (3.8%) had died: one in an accident, two from physical diseases and three because of poor care. Ninety-five (60.9%) still remained without treatment.

Of 95 cases, 12 had recovered, while two patients relapsed during the 2-year follow-up. The relapse rate was 8.3% per year.

At the end of follow-up period, the clinical outcome of 95 patients with schizophrenia who had not received treatment showed that there were 10 patients (10.5%) whose illness was in complete remission, 11 patients (11.6%) whose illness was in partial remission, 68 patients (71.6%) whose illness still maintained marked symptoms, and six patients (6.3%) whose illness had deteriorated. There was no significant difference in clinical status between baseline (Time 1) and follow-up (Time 2) ($P > 0.05$).

DISCUSSION

The findings show similarities between the total prevalence rate of schizophrenia in this study (4.13 per 1000) and that for the

rural areas in the survey carried out in 1982 (4.26 per 1000).

Davis & Andriukaitis (1986) reported that the natural course of schizophrenia is poor in the absence of consistently effective and broadly applied treatment, about two-thirds of patients with schizophrenia remain symptomatic. The results of this study showed that 30.6% of patients with schizophrenia received no treatment at all among the population of people with schizophrenia in a rural area of China. The main reasons for not receiving treatment were lack of money and relatives not perceiving the patients to be suffering from a mental illness. For these patients, their mean age was older and duration of illness was longer than those receiving regular treatment. Most untreated patients (75.6%) continued to experience marked symptoms, and some (6.4%) experienced a further deterioration in their illness. Social functioning was damaged severely and social disability was quite strongly correlated with clinical outcome. Our original expectancy was that the natural course of schizophrenia would be favourable in a rural area of China. In every instance, however, the results also supported the conclusion that the natural course of schizophrenia, especially clinical outcome, was poor – even in a Chinese rural area. Compared with patients who received treatment for schizophrenia, the results of this study still suggested that the natural outcome of schizophrenia was heterogeneous and poor in the rural area studied. Antipsychotic drug treatment, particularly when received regularly, may be very important in improving the prognosis of these patients.

Belitsky & McGlashan (1993) once reported that there was strong evidence that deterioration in schizophrenia generally occurs earlier rather than later in the disorder's natural history and is typically not relentlessly progressive. Schizophrenia with many negative symptoms has been thought to be associated with poor premorbid functioning, insidious onset and partial or no remissions during the first several years of illness, and in most cases a progressive course leading to permanent disability. Patients with the poorest long-term outcome tend to show an increase in negative symptoms during the early years of their illness (Fenton & McGlashan, 1991). Wyatt (1991) showed that early intervention with neuroleptics in patients with first-episode schizophrenia increased the likelihood of

an improved long-term course. In our study, we found that no patients deteriorated in the first year. Deterioration developed gradually after 1 year. The deterioration rate was maintained at a specific level, and did not increase significantly after 2 years. This result indicates that not all patients with schizophrenia will experience deterioration in their mental health by the end of the illness. Schizophrenia remains a severe disorder that can be chronic and, in a proportion of patients, unremitting throughout life. Therefore, intervention for schizophrenia, including psychosocial intervention and medication, should occur during the early stages of the illness.

A gender effect on the course of illness has been suggested in this study. Females had a significantly better clinical outcome than males ($P < 0.05$). That women had a better outcome than men, was also reported in India (Verghese *et al*, 1989). Oestrogen has been thought to play a protective, that is, neuroleptic-like, role in the disease process of schizophrenia, resulting from a hypothesised antidopaminergic effect that could delay the development of the illness (Seeman, 1982; Seeman & Lang, 1990). Bilder *et al* (1992) used the 'hold' test of the Wechsler Adult Intelligence Test-Revised to determine the degree of intellectual deterioration in schizophrenia and found significantly greater deterioration among men than women. Apart from biological factors, we consider that culture might have an effect on this result. Females in Chinese rural areas take on most of the housework, taking care of their children, and some farm work, despite suffering from schizophrenia. We suggest that working and exercising social functioning in patients with schizophrenia has a strong effect on preventing deterioration and improving the prognosis of the illness.

Even though 82.1% of patients still retained marked symptoms, 77.6% of the patients in the never-treated group could still do full- or part-time work. The occupational functioning of these patients was comparatively good. This result shows that any decrease in work ability caused by the illness did not correspond with the severity of symptoms of the illness. The patients who had marked psychotic symptoms could still do general housework or farm work in the rural area. Therefore, even patients who have psychotic symptoms should not be restricted in work. The importance of work as a prognostic variable

was also reported in another Indian study (Kulhara *et al*, 1989).

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REFERENCES

Belitsky, R. & McGlashan, T. H. (1993)

The manifestation of schizophrenia in late life: a dearth of data. *Schizophrenia Bulletin*, **19**, 683–685.

Bilder, R., Lipschute-Broch, L., Reiter, G., et al (1992)

Intellectual deficits in first episode schizophrenia: evidence for progressive deterioration. *Schizophrenia Bulletin*, **18**, 437–448.

Black, D. W., Warrack, G. & Winokur, G. (1985)

The Iowa Record-Linkage Study, I: Suicides and accidental deaths among psychiatric patients. *Archives of General Psychiatry*, **42**, 71–75.

Cooper, J. E. & Sartorius, N. (eds) (1996)

Mental Disorders in China: Results of the National Epidemiological Survey in 12 Areas. London: Gaskell.

Davis, J. M. & Andriukaitis, S. (1986)

The natural course of schizophrenia and effective maintenance drug treatment. *Journal of Clinical Psychopharmacology*, **6** (suppl.), 2S–10S.

Edgerton, R. B. & Cohen, A. (1994)

Culture and schizophrenia: the DOSMD challenge. *British Journal of Psychiatry*, **164**, 222–231.

Fenton, W. S. & McGlashan, T. H. (1991)

Natural history of schizophrenia subtypes. II. Positive and negative symptoms and long-term course. *Archives of General Psychiatry*, **48**, 978–986.

Kulhara, P., Avasthi, A. & Chandiramani, K. (1989)

Prognostic variables in schizophrenia. *Indian Journal of Psychiatry*, **31**, 51–63.

Landmark, J., Cernovsky, Z. Z. & Mersky, H. (1987)

Correlates of suicide attempts and ideation in schizophrenia. *British Journal of Psychiatry*, **151**, 18–20.

Leff, J., Sartorius, N., Jablensky, M., et al (1991)

The international pilot study of schizophrenia: five-year follow-up findings. In *Search for the Causes of Schizophrenia*, Vol. 2 (eds H. Hafener & W. F. Gettaz). Berlin: Springer-Verlag.

CLINICAL IMPLICATIONS

■ The natural course of schizophrenia, especially clinical outcome, was poor in this rural Chinese area.

■ For people with schizophrenia, some form of treatment, especially regular antipsychotic medication, is better than no treatment at all.

■ Occupational functioning in relation to schizophrenia did not correspond with symptom severity.

LIMITATIONS

■ More detailed measures should be conducted at 2-year follow-up

■ Measurement scales should be more comprehensive.

■ Longer-term follow-up of these subjects is desirable.

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Salokangas, R. K. R. (1983) Prognostic implications of the sex of schizophrenic patients. *British Journal of Psychiatry*, **142**, 145–151.

Sartorius, N., Jablensky, A. & Shapiro, R. (1977) Two years follow-up of the patients included in the WHO International Pilot Study of Schizophrenia. *Psychological Medicine*, **7**, 529–541.

Seeman, M. V. (1982) Gender differences in schizophrenia. *Canadian Journal of Psychiatry*, **27**, 108–111.

— & **Lang, M. (1990)** The role of estrogen in schizophrenia gender differences. *Schizophrenia Bulletin*, **16**, 185–194.

Shen, Y. & Wang, C. (1985) *A Handbook of Epidemiological Investigation of Mental Illness*, pp. 11–31, 42–67. Beijing: Renming Health Press.

—, **Chen, C., Zhang, W., et al (1986)** An epidemiological investigation on mental disorders in 12

regions of China: Methodology and data analysis (in Chinese). *Chinese Journal of Neurology and Psychiatry*, **19**, 65–69.

Verghese, A., John, J. K., Rajkumar, S., et al (1989) Factors associated with the course and outcome of schizophrenia in India. Results of a two-year multi-centre follow-up study. *British Journal of Psychiatry*, **154**, 499–503.

Waxler, N. E. (1979) Is outcome for schizophrenia better in non-industrial societies: the case of Sri Lanka. *Journal of Nervous and Mental Disease*, **167**, 144–158.

Wyatt, R. J. (1991) Neuroleptics and the natural course of schizophrenia. *Schizophrenia Bulletin*, **17**, 325–351.

Yang, D. S. (1989) *Chinese Classification and Diagnostic Criteria of Mental Disorder and Cases*, pp. 502–578. Changsha: University of Hunan Press.