Original Research

Twenty-Year Course of Schizophrenia: The Madras Longitudinal Study

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Objective: To follow up 90 first-episode schizophrenia patients after 20 years and to study the course of symptomatology, work, social functioning, and pattern of illness during this period.

Methods: The Present State Examination and the Psychiatric and Personal History Schedule were administered at fixed points during follow-up. The measures adopted to ensure a good follow-up rate (67%) after 20 years under adverse conditions are described.

Results: Complete data were obtained from 61 subjects; 16 had died, and 13 could not be traced. After 20 years, 5 patients had recovered completely, and another 5 were continuously ill. Most of the cohort had multiple relapses with or without complete remission between them. The Global Assessment of Functioning Scale showed that symptoms and social functioning in this sample approximated results from developing countries and were much better than those of developed nations. There were not many sex differences. Marriage and occupational rates were higher than those observed in many published reports.

Conclusions: This is one of the few long-term follow-up studies from the developing world. It reveals a pattern of course and functioning distinctly better than that found in many such studies from the developed nations.

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Information on funding and support and author affiliations appears at the end of the article.

Clinical Implications

- A 20-year follow-up of first-onset schizophrenia patients helps in understanding the longitudinal course of symptoms and the impact of interventions on them.
- Studies of social functioning that include work and marriage will help the planning of rehabilitation strategies.
- The rather high mortality rate draws attention to the effects of suicide, poor living conditions, and comorbidity in the study subjects.

Limitations

- The follow-up was both prospective and retrospective.
- A single rater was involved throughout the study.
- The results have limited generalizability.

Key Words: *schizophrenia, follow-up studies, pattern of course, mortality, work*

Ever since Bleuler published his account of nearly a lifetime's work with schizophrenia patients (1), there has been great interest in studying the long-term course of this illness. The evolution of schizophrenia's conceptualization from dementia praecox to a heterogeneous disorder with variable outcomes has been well documented. The multinational International Pilot Study of Schizophrenia (IPSS; 2) initiated by the World Health Organization (WHO) showed that it is eminently possible to use the same standardized criteria and instruments to compare the course and outcome of schizophrenia in different countries and cultures.

Among the few studies with more than 15 years of follow-up have been those of Tsuang and Winokur (3), De Sisto and others (4), Huber and others (5), and Moller and others (6). However, the varying nature and size of the samples, the varying duration of follow-up, and the lack of uniform definitions

of outcome make comparison difficult. More recently, the International Study of Schizophrenia (ISOS) reassessed the samples included in the original WHO studies, with follow-up periods ranging from 13 to 26 years. Field and coordinating centres have published data from these reassessments (7–10).

One of the most exciting findings of many cross-cultural studies was that of better outcome in developing countries, as indicated by data from the IPSS (2). A more recent publication, which examined this finding in light of the ISOS reassessment of the original WHO studies cohort, also reported evidence of a better course of illness in developing countries (8). However, the authors discuss possible biases, especially those termed as cultural factors.

This paper reports on the Madras Longitudinal Study. One of the very few follow-up studies of first-episode schizophrenia from this part of the world, it has completed a 20-year follow-up of these patients and obtained a wealth of data on clinical, social, economic, and family dimensions. It describes the course of illness, symptom profile, and occupational functioning over the 20-year period.

Material and Methods

The 1981–1982 study included 90 first-episode schizophrenia patients fulfilling ICD-9 criteria. At the end of 20 years, it was possible to complete all assessments on 61 subjects. This paper analyzes information from these 61 subjects.

The periodicity of follow-up varied. While monthly assessments were possible during the first 10 years, they could not be maintained further, owing to lack of funding. The attempt to follow up the entire cohort after 20 years was initiated in 2001 and completed in early 2002.

Study Site

The original study site was the Department of Psychiatry, Madras Medical College, an active outpatient department with limited admission facilities. It is located in Chennai, a city in south India that has a population of approximately 6 million. Follow-up for the first 5 years was effected from this site. Further follow-up was done at the Schizophrenia Research Foundation, a voluntary organization involved in care and research into chronic mental illness. The 10-year data were analyzed at the Johns Hopkins Institute as part of a collaborative venture (11–13). The sample was also included in the WHO-coordinated ISOS (7).

Instruments

Informed consent was obtained from all subjects and their families. The following measures were administered at baseline and at subsequent assessments, as indicated:

1. Present State Examination, 9th edition (PSE-9): The data were grouped into 33 syndromes that were used in the analysis.

2. Psychiatric and Personal History Schedule (intake and follow-up versions), which elicited demographic and historical variables.

3. The Interim Follow-Up Schedule, which recorded major symptoms derived from the PSE-9, together with treatment details, including drug compliance. This was used on all subjects every month for the first 10 years.

4. At the end of year 20, the Global Assessment of Functioning (GAF), which measures both symptoms and functioning, was completed for all subjects. The GAF is a diagnostic criterion for Axis V according to the DSM-III (14). It assesses symptoms and overall functioning on a scale of 1 to 100, with higher scores indicating fewer symptoms and better functioning.

5. Interviews with patients and caregivers, along with case notes whenever available, to complete the assessments. Information on treatment taken during this period was also collated. The author carried out all the assessments made at the end of 20 years.

Operational Definitions

"First episode" was defined as the first appearance of psychotic symptoms leading to first contact with a medical health service. "Remission" was defined as the total absence of all positive and negative symptoms for a period of at least 1 month. "Relapse" was defined as the reappearance of 1 or more positive psychotic symptoms after 1 month of total remission.

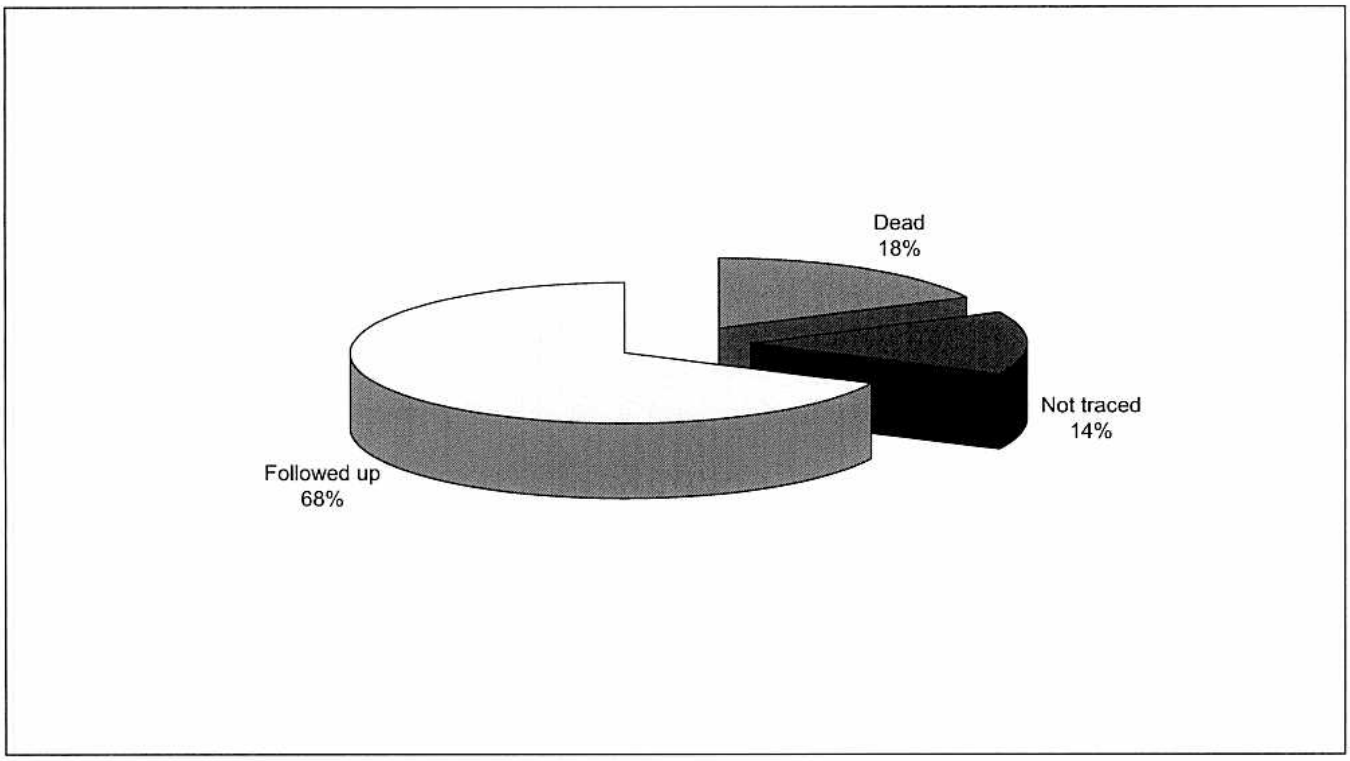
Results

Characteristics at Inclusion (1981–1982)

This was a predominantly urban sample of 90 first-episode patients with an equal sex distribution (men = 45, women = 45). This distribution happened not by design, but by chance. The mean age of the sample was 24.5 years, with age ranging from 17 to 38 years. The age of onset did not differ between the sexes. Only 15/90 subjects (16.7%) had never been to school. The sample averaged 10.8 years of education. Most subjects were from lower- and middle-income groups. All patients lived with their families, of which 79% were nuclear and the rest extended and joint. Most of the women were full-time housewives; 3 were students.

About 60% of the sample were not married, and 69% had their onset of illness before age 24 years. Insidious onset was seen in 54.5% (49 subjects). Sixteen subjects had a family history of psychosis.

Figure 1 Twenty-year follow-up



Characteristics at the End of 20 Years (2001–2002)

Follow-Up. All assessments were completed for 61 of the 90 subjects originally included (men = 33, women = 28), giving a follow-up rate of 67.7%. Sixteen patients (17.7%) had died during this period; 7 had moved outside the city; and 2 had wandered away, never to be traced again. The remaining 4 had moved without leaving any contact address and also could not be traced (Figure 1).

Deaths. Of the 16 deaths, 7 (men = 4, women = 3) were suicides. The other causes of death were physical illnesses such as tuberculosis, severe gastroenteritis, and unknown fevers. Because postmortem examinations were not done, it was not possible to determine the actual cause of death in some cases. Hanging, self-immolation, and ingestion of poison (specifically, pesticides) were the common modes of suicide. One subject just walked into the sea. If the deceased subjects are taken into account, the follow-up rate rises to 82%.

Clinical Picture. On the PSE-9 administered at the end of 20 years, 36 subjects (59%) were asymptomatic at the syndromal, but not at the symptom, level. It should be kept in mind that the time frame of the PSE-9 is 1 month before interview.

Compared with baseline, all syndromes registered a decline, although some, such as slowness, loss of interest, concentration, and simple depression, registered an increase over 10 years (Table 1). Between years 10 and 20, positive symptoms showed little difference.

Of the subjects, 5 men and 9 women (23%) had attempted suicide. The prevalence of alcohol abuse was very low, with only 15% reporting it. Only 2 patients abused drugs. All but 2 patients lived with families. Nearly 30% had a worsening of their socioeconomic status during the 20-year period. Only 11 families reported dangerous or harmful behaviour. At the end of 20 years, 73.7% of subjects were married, with only 16 patients remaining single.

Treatment. Nearly one-half of the 61 patients followed up (n = 29, 47%) were not in treatment at the end of 20 years. Of these, 14 had been clinically stable for the 2-year period preceding assessment (men = 4, women = 10). Fifteen (all men) were ill but refused medication for various reasons. Two were living alone and 1 reported a problem with access to the facility. Of the 15 men who were ill and refused medication, 10 (66.6%) were single and either living alone or with elderly parents. In contrast, none of the women who had stopped medication were symptomatic.

Hospitalization. Despite the large number of relapsed patients in the sample, there were few rehospitalizations. During the entire 20-year period, only 22 subjects were hospitalized, and the average length of stay was 10.6 months. Two subjects were in a prolonged-stay ward.

GAF. In this sample, 47 subjects (77.1%) had a GAF-Symptoms score of over 60, and 45 (73,8%) had a GAF-Functioning score of over 60. Although more men had lower scores, this difference was not statistically significant.

Table 1 Present State Examinations at intake, 10 years, and 20 years

Syndrome	Intake	10 years	20 years
	Number of patients		
Nuclear syndrome	51	2	8
Catatonic syndrome	15	0	0
Incoherent speech	23	0	2
Residual syndrome	18	11	5
Depressive delusions	9	1	0
Simple depression	51	3	21
Obsessional syndrome	4	0	0
General anxiety	9	0	1
Situational anxiety	2	1	0
Affective flattening	30	8	9
Hypomania	13	0	1
Auditory hallucinations	27	9	10
Persecution delusions	35	10	8
Reference delusions	45	1	9
Religious delusions	11	0	1
Sexual delusions	31	0	2
Visual hallucinations	8	0	0
Olfactory hallucinations	2	0	0
Overactivity	4	2	5
Slowness	35	7	19
Self-neglect	16	8	13
Loss of interest	52	0	22
Other symptoms	41	1	10
Subclinical delusions or hallucinations	0	0	0

Pattern of Course. The pattern of course during the 20-year period was studied in great detail. There were 4 basic patterns: complete remission, few residual symptoms, relapses with and without complete remission, and continuous illness (Figure 2). It can be seen from Figure 2 that the best and the worst groups had 5 subjects each, while most had a course characterized by relapses with or without complete remissions between them. In the 20-year period, more than 80% of the original cohort experienced relapses, with nearly one-half of the relapses occurring between years 10 and 20. The number of relapses occurring between years 1 and 10 did not differ significantly from those occurring between years 10 and 20.

Dropouts and Deaths: Possible Bias. Sixteen patients died, and 13 were lost to follow-up. The characteristics of these 16 patients at the beginning of the study and at their last recorded follow-up did not differ significantly, compared with the group at 20-year follow-up. This finding eliminates any bias that could have been caused by this subsample.

Occupation. Of the 28 women, 21 were either full-time housewives or unmarried girls living with their parents and having varying domestic responsibilities. One worked full-time, and 6 had held jobs intermittently. Only 6 men remained unemployed during the entire 20-year period. Nine held jobs continuously, while the remaining 18 had employment periods ranging from 5 to 220 months. At the end of year 20, 25/33 men were employed (76%). Nearly one-half had full-time jobs under normal conditions, and the others worked part-time or in a family business. Over two-thirds of those who worked had minimal or no dysfunction at work.

Discussion

This sample has provided a unique opportunity to study the course of illness and assess clinical and social parameters at the end of 20 years in a cohort with first-episode schizophrenic illness.

Follow-Up

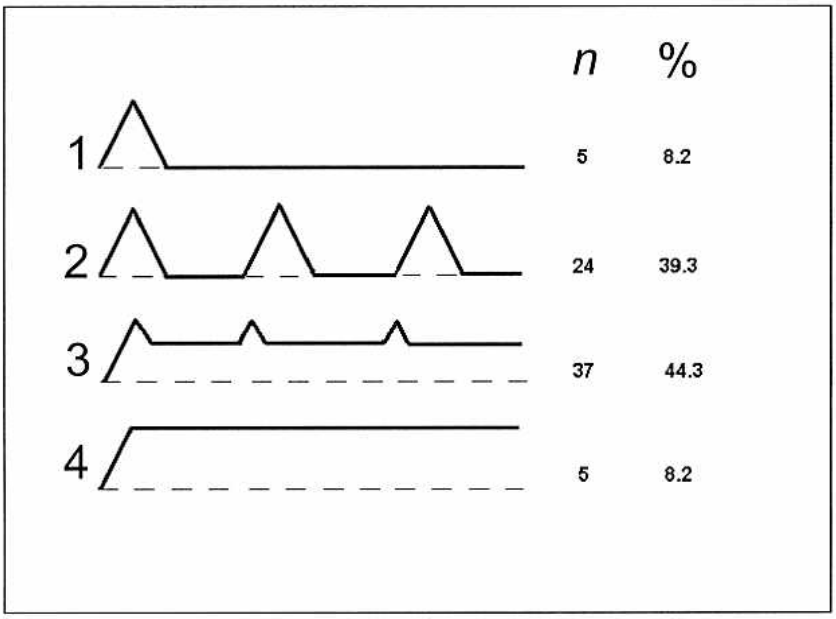
In the ISOS, developed-nation studies also had a follow-up rate of 67% (8), but the similarity probably ends there. In our sample, the follow-up rate of 67% is indeed heartening, considering the resources available to us. In this country, it is not mandatory for people from lower socioeconomic groups who shift homes to inform anybody, least of all the health care system. There are no guidelines in the postal department and no movement registers. The persuasive ability of the field staff, who sometimes had to make as many as 6 or 7 trips to locate a single individual, was largely responsible for the good follow-up rate. This process was especially difficult in the case of women who married after inclusion in the study. In almost all cases, the fact that the bride suffered from mental illness was not disclosed to the groom or his family; hence, her parents were very reluctant to give us her address and forbade any house visits. Most interviews were completed only when the woman visited her parental home.

Although some of the PSE-9 syndromes registered an increase at the 20-year point, we nevertheless wish to reiterate previously published observations (2) that the perception of progressive deterioration in schizophrenia is no longer tenable, considering that only 5/61 patients were continuously ill. However, the data also do not conform to some observations that the course of schizophrenia plateaus after 5 years, with little variability after that period.

Sex Differences

There were no sex differences in the pattern of course or symptom profile. Several studies in the 1970s and 1980s observed sex differences in symptomatology. However, in their recent study of 239 patients, Usall and others found no

Figure 2 Patterns of course



1 = Complete remission
2 = Relapse with complete remission in between
3 = Relapse with partial remission in between
4 = Continuous illness

differences in symptomatological variables (according to either global or separate Positive and Negative Syndrome Scales) or in type and course of schizophrenia (15). Occupational status differed markedly between the sexes, with most of the women being full-time homemakers.

Mortality

Mortality was high in our sample (10% in 10 years and 17% in 20 years). The average age of death was 34.2 years, which is much below the current average lifespan in India (60.5 years). This mortality rate is much higher than reported rates from developed countries: 13.6% (16), 3.3% (9), and 11% (10). Leon's figures from a developing economy also report a low rate of 2% over a 10-year period (17).

It must be borne in mind that this sample was largely from lower-middle and poorer economic classes, and many either did not identify the physical illness or did not have the means to obtain prompt and regular treatment. Suicides accounted for 7/16 deaths, all of them under age 35 years. In another Indian study, poor course of schizophrenia at the end of 2 years was found to be associated with poor course at 15-year follow-up and high mortality, with 47% of the subjects dead at the end of 15 years (18).

The GAF Symptom and Functioning scores very closely approximate the scores for developing countries in the ISOS incidence sample (7). This reiterates the finding that, despite a course of illness marked by several episodes with remissions of variable nature, the outcome in developing countries, in terms of both clinical symptoms and social functioning, is distinctly superior to that observed for schizophrenia patients in the developed countries. Of course, the actual reasons for this difference are still undetermined, with various factors such as social and family support, better tolerance, and biological differences remaining as postulates only.

Occupation

A significant finding of this study has been the high employment rate of over 75% among the men at the end of 20 years of illness. A similar figure was also observed at the end of 10 years (19). This rate is much higher than that reported from the West (20,21).

A 15-year follow-up of Chinese schizophrenia patients found that at the end of 5, 10, and 15 years the percentages of patients still able to work were 55%, 54%, and 48%, respectively (22)—figures certainly comparable with the data from this current study.

The high employment rate is possibly owing to several factors. The sample was largely low- and middle-class, and it was not too difficult for them to find jobs in the unorganized sector (for example, as street vendors, sales staff in shops, and domestic help). Absence of state social security benefits and pressure to find work as primary wage earners would also have contributed to the high rate of employment.

The fact that all assessments were made by a single rater (the author) could be a study limitation. While enhancing reliability, this may threaten validity. As well, it was not possible to obtain more details about the deaths of the 16 deceased patients, since in many cases the families were not able to produce any medical records.

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Résumé : L'évolution de la schizophrénie en vingt ans : l'étude longitudinale de Madras

Objectif : Assurer le suivi, 20 ans après, de 90 patients ayant souffert d'un premier épisode de schizophrénie et étudier l'évolution de la symptomatologie, du travail, du fonctionnement social et du modèle de la maladie durant cette période.

Méthodes : L'examen de l'état actuel et l'échelle et le questionnaire sur les antécédents psychiatriques et personnels ont été administrés à des points fixes durant le suivi. Les mesures adoptées pour assurer un bon taux de suivi (67 %) après 20 ans dans des conditions défavorables sont décrites.

Résultats : Des données complètes ont été obtenues de 61 sujets; 16 étaient décédés, et 13 n'ont pu être retrouvés. Après 20 ans, 5 patients étaient complètement rétablis, et 5 autres étaient continuellement malades. La majeure partie de la cohorte avait eu de multiples rechutes, avec ou sans rémission complète entre elles. L'échelle d'évaluation globale du fonctionnement indiquait que les symptômes et le fonctionnement social de cet échantillon s'approchaient des résultats des pays en voie de développement, et étaient beaucoup meilleurs que ceux des pays développés. Il n'y avait pas beaucoup de différences entre les sexes. Le mariage et les salaires professionnels étaient plus élevés que ceux observés dans de nombreux rapports publiés.

Conclusions : Il s'agit d'une des quelques études de suivi des pays en voie de développement. Elle a révélé un modèle d'évolution et de fonctionnement nettement supérieur à ceux de nombreuses études semblables des pays développés.