Differences in the process of diagnosis in males and females were further manifested both in the number of admissions and length of time between first admission and the diagnosis of schizophrenia. The majority of readmissions and the longest interval occurred in females, and this in those with the first-admission diagnosis of affective psychosis. A reason for this might be that first-admission diagnoses of unipolar depression (296.2, ICD–8) and involutional melancholia (296.0, ICD–8) were more frequently made in females, whereas cyclic manic–depressive psychoses (296.3, ICD–8) were more so in males.

The present findings indicate that schizophrenic males and females differ not only with regard to age and diagnosis at first admission, they also differ with respect to diagnostic process. However, admission is known to be affected by many diverse factors. The practice in Croatia is for patients with manifest psychoses to be admitted: the main criterion then applied to such patients is the feasibility of providing out-patient medical and psychiatric treatment and/or social support either at an institution or home, which can be different for the two sexes. The recording of schizophrenic admissions also depends on information source, method of collection, and processing.

Although admission-based statistics, PCRC data included, point to a higher female age at first admission, the question of whether age differences between males and females at the time of disease onset are genuine is still hypothetical. Thus the question now posed is whether the characteristics derived from such hospital statistics in fact describe stages of the disease other than disease onset. In studying the aetiology of schizophrenia in relation to age at onset, epidemiological studies are required. Such a study is reported in the following paper (this issue, pp. 368–372).

Age of Disease Onset in Croatia's Hospitalised Schizophrenics

V. FOLNEGOVIĆ-ŠMALC, Z. FOLNEGOVIĆ and Ž. KULČAR

Age at onset was determined in a sample of 360 patients representative of the 8069 schizophrenics hospitalised in SR Croatia. The 95% confidence interval for mean age at onset was 22.9–26.7 years. The difference between males and females was not significant, unlike the age difference between the sexes reported for age at first admission for schizophrenia. Results may be influenced by attrition of the original population of patients.

Epidemiological studies of schizophrenia have increasingly emphasised (Strömgren, 1987) that hospital statistics have some deficiencies when used in studies of incidence rates of schizophrenia, particularly when describing the characteristics of cases. A number of factors, such as the level of development and accessibility of mental health services and patients' socioeconomic status, have been noted to affect admission rates. In view of the diversity of these factors, the validity of the cross-cultural comparability between populations has been questioned (ten Horn, 1986; Jennings, 1986). Differences in diagnostic processes and criteria may also be significant contributing factors (Häfner & an der Heiden, 1986; Sartorius et al, 1986; Sartorius, 1988). Thus, there is a justified emphasis on the need to supplement and correct hospital statistical data with epidemiological findings and from long-term

(or even lifelong) follow-up studies (World Health Organization, 1984).

The Psychotic Case Register of Croatia (PCRC) has produced data indicating that schizophrenic females are older than males at first admission, and that of those admitted with schizophrenia for the first time, males comprise a disproportionate number of the younger age-group, and females of the older age-group (second paper, this issue, pp. 365–368).

A question arising in this connection is whether the PCRC realistically depicts the characteristics of schizophrenic cases, i.e. whether the onset of the disorder in females does indeed occur at a later age than in males, as also reported by Strömgren (1987), or whether these characteristics are due to differences in its course and outcome and/or to the cumulative effect of other factors.

We are conducting an epidemiological lifelong follow-up study of a representative sample of schizophrenic cases selected from the PCRC. This includes information on age at onset and at first admission.

Method

The present results are based on an epidemiological, (life-long) follow-up study – both retrospective and prospective – of a representative sample of Croatia's schizophrenic patients. The base population for selection of the sample consisted of 10 569 CPCR-recorded patients who had been admitted to hospital and diagnosed as schizophrenic over the period 1962–71, regardless of possible previous admissions. Excluded from this population were all those who died in hospital during this period, those aged 55 or over before 1974, and patients with an additional diagnosis of oligophrenia. This yielded a sample of 8069 patients.

The study sample was derived using a two-stage random sample of sets. At the first stage, 52 patients were selected at random, while at the second, 'selection units' were formed, comprising groups of patients geographically closest to each other, by residential address. Standard sample theory required at least eight patients per unit, assuming that at least some distributions were normal. (More detailed descriptions of the sample selection and expansion formula are given in the project's final report (Kulčar et al, 1983).) However, a pilot study showed that eight patients per unit was too few, as around half the subjects were not to be found at the recorded address (unknown there, moved, unavailable, dead, etc.), and the size of the selection units therefore had to be raised to 16 patients each.

During 1973, medical students who had been especially trained for the study carried out a field survey to obtain case histories. These were derived from descriptions from both patients in the sample and their families (and sometimes the wider community), resulting in a collection of relevant information for 449 sample cases (out of a possible $52 \times 16 = 832$ cases).

Next, past medical histories were constructed for every such patient based on data from both admitting institutions and from general practitioners. Between 1973 and 1975, these patients were psychiatrically examined wherever they were living – home, hospital, or social institution.

All patients were rediagnosed after this psychiatric examination and inspection of their previous medical records. ICD-8 (World Health Organization, 1967) and compatible assessment and diagnostic scales (Wing et al, 1974) were also used; staff had received appropriate training for this as part of a collaborative study by the World Health Organization (1988).

This rediagnosis produced a non-confirmation of the diagnosis of schizophrenia in 22 patients (5%), 17 of whom had had only a single admission. An additional 17 diagnoses could not confidently be either confirmed or rejected, and this group was put on a 'waiting list' to be incorporated in a subsequent follow-up. Eight patients died in the interval between the student interviewer's visit and the psychiatric examination. This left 402 cases for analysis.

The following parameters were assessed: status at psychiatric examination, type of treatment received, socio-economic status, social functioning, and the course of the disease. These patients, as well as the 17 waiting-list patients, were re-examined by research team psychiatrists during the period 1987–89, when, in addition, cause of death, place of death, and circumstances preceding it were recorded for deaths, where appropriate. An analysis of the 1987–89 data is in preparation.

Both patient and family recollections and the medical records were used as the basis for determining age at onset and age at first admission, independent of either the diagnosis recorded at the time, the nature of the admitting institution, or the place where this occurred (e.g. foreign country or military hospital).

The age of onset of the disorder is here defined as either the time when certain behavioural changes were noted by the patient or his family, or the point where failure to function socially first became noticeable. While the timing of onset of schizophrenia could be determined with the necessary precision in 360 cases, this was not possible in 42 cases, because of missing records or inadequate information at interview. Consequently, the present paper relates to those 360 patients.

Results

The age range for onset of schizophrenia was 9–48 years (mean 24.8 ± 8.1 years, median 23.8 years). Given the standard error of 0.978 years, the 95% confidence interval for mean age is 22.9–26.7 years. The difference in the average age of onset between males and females was not significant ($P > 0.05$) (Table I).

We also examined the time between the onset of disease and first admission (Table II). In 65% of the cases, the first admission took place within two years of onset; in 7.8%, however, this interval exceeded ten years. The proportion of patients ill for over ten years before admission was significantly higher among females ($P > 0.05$).

TABLE I

Age at disease onset in a sample of 360 schizophrenics

Age (years)	Percentage of whole sample		
	total	male (n = 192)	female (n = 168)
≤14	9.4	9.9	8.9
15–19	23.9	21.9	26.2
20–24	22.2	26.6	17.3
25–29	16.7	13.5	20.2
30–34	15.6	16.2	14.9
35–39	8.1	7.3	8.9
40–44	3.6	3.6	3.6
45–49	0.6	1.0	—
Means ± s.d.	24.8 ± 8.1	24.8 ± 8.2	24.9 ± 8.1

Difference between sexes, Student's t-test, $P = 0.07$, NS.

TABLE II

Interval between onset and admission in a sample of 360 schizophrenics

Interval between onset and admission (years)	Percentage of whole sample		
	total	male (n = 192)	female (n = 168)
≤2	65.0	66.1	63.7
2–5	16.9	19.3	14.3
5–10	10.3	9.9	10.7
10+	7.8	4.7[+]	11.3[+]

Difference between sexes, $\chi^2 = 6.51$, d.f. $= 3$, $P < 0.05$.

Discussion

The onset of the disorder was readily determined in those schizophrenics who had experienced neither an insidious course nor gradual failure in social functioning. These were mostly catatonic-type cases in which stupor or catatonic agitation had occurred over a day or two, or those in which onset was marked by homicide or attempted suicide – both of which are fairly common at the initial stage of the disease (Glaser, 1934). Onset was also determined precisely for those cases beginning with paranoid hallucinations.

In cases of insidious onset, however, and particularly those beginning in adolescence, it was sometimes difficult to differentiate between pre-morbid personality features and disease symptoms. This was common in cases displaying a hebephrenic or simplex type of onset. In such cases, the family or members of the wider community generally reported the beginning of the patient's failure to function socially as the onset of disease, though rarely recognising

particular symptoms. As described by patients themselves, the onset of the disease was often marked by a "feeling of having changed", pointing to depersonalisation as one of the first symptoms.

Our results showed that the average age of patients in this sample at the onset of schizophrenia was 24.8 years, and that there was no difference between males and females in this respect. However, for females the interval between onset and first admission was longer.

Those long intervals which occurred between onset of the disorder and first admission arose because most schizophrenics had no insight into their condition, and hence perceived no need for treatment. It was therefore rare for the first contact with the mental health services or first admission – the latter still being a necessary condition for treatment at the acute stage in this republic – to result from the patient's own initiative. Consequently, apart from being determined by the nature of disease proper, admission is determined by a number of other factors, including the reactions of the family and the wider community, and development of mental health and social services, etc.

The influence of community attitudes on the timing of admission can be seen in the data of this paper which show that the interval between onset and admission is shorter the more abrupt the onset and the more strikingly pathological the symptoms; it is also shorter in cases showing manifest aggressiveness or suicidal tendencies (Folnegović-Šmalc, 1979). Case recognition, and even first admission, are further dependent on 'barriers'. These primarily consist of the role of, and obligations imposed on an individual in society; they are a function of age and expected levels of social status and social functioning. This was supported by the findings that time before admission was longer in rural areas, for patients of lower educational attainment, and for the unemployed. The present finding that the interval between onset and admission was longer for females than for males must also be regarded in the light of the differences in their social statuses, roles, and obligations in our population.

It should be emphasised that this study outlines the characteristics of schizophrenics in the community. In fact, 16% of those detected during screening for functional psychoses in a representative sample of Croatia's population (Kesić et al, 1981) had not been admitted to hospital at any stage. The majority of these had had no previous contact with the mental health services despite the fact that in some cases, the disease had already lasted over 20 years. The proportion of the sample not admitted has been reported to be 3.4 times as high in females as in males (Folnegović-Šmalc et al, 1980).

It is therefore possible for the interval between onset and admission to vary, depending on a number of factors, reflected in the slightly higher female age at first admission, despite the fact that in both sexes, onset occurred, on the average, at the same age. The characteristics of cases at the time of recognition may therefore be different from those present at the time of onset. These differences would also be influenced by the method of collecting of information. From the PCRC's standpoint, they are influenced by: the proportion of cases who were first admitted either in other Yugoslav republics or abroad; the interval between the first and second admission, which in some cases is over ten years; a proportion of schizophrenics with the diagnosis, at the first and even several subsequent admissions, of other psychoses or even of other mental disorders (neurosis, psychopathy, alcoholism, drug dependency, etc.). There are also problems in relation to recording every admission for each patient, maintaining longitudinal follow-up via the register, and reduction of the diagnostic coverage, which in some cases allowed one of the readmissions to be entered as the first admission. Moreover, some other diagnoses (including post-partum psychosis) were quite frequently given to female schizophrenics at first admission, and the process of diagnosing schizophrenia took longer for females. The age differential at first admission between males and females thus became even larger. In fact, as they were older at first admission, females more often received a diagnosis of affective or organic psychosis. Conversely, being younger, males were more often diagnosed as schizophrenic.

Differences between male and female case characteristics may also be a reflection of different course and outcome. Apart from possible variations in the natural course of the disease, differences in the rates of symptomatic alcoholism, other mental and somatic diseases, mortality, migration etc., may also be significant in this respect. The probability of recognition of schizophrenia in males and females respectively in a population can differ in line with the above factors. This should be allowed for when differences in the course and outcome of recognised cases are being considered.

Conclusion

The onset of schizophrenia in males and females occurred at approximately the same age. Moreover, sex differences at first admission resulted primarily from a number of social factors. Hospital statistics are inadequate for studying the characteristics of schizophrenic patients at disease onset and, in this connection, for studying aetiology itself; this points to the need to check hospital statistical data with special epidemiological investigations.

References

ASTRUP, C. (1982) *The Increase of Mental Disorders*. Unpublished Manuscript, the National Case Register of Mental Disorder, Oslo, Gaustad Hospital. (Cited by Häfner & an der Heiden (1986).)

BROOKE, E. (1974) *The Current and Future Use of Registers in Health Information Systems*. WHO Offset Publication no. 8. Geneva: WHO.

COOPER, J. E., GOODHED, D., CRAIG, T., et al (1987) The incidence of schizophrenia in Nottingham. *British Journal of Psychiatry*, 151, 619–626.

DUPONT, A. & WEEKE, A. (1977) Antalet af psykiatriske indlæggelser i Danmark. *Ugeskrift for Läger*, 139, 1241–1242.

EAGLES, J. M. & WHALLEY, L. J. (1985). Decline in the diagnosis of schizophrenia among first admissions to Scottish mental hospitals from 1969–78. *British Journal of Psychiatry*, 146, 151–154.

FOLNEGOVIĆ, Z., FOLNEGOVIĆ-ŠMALC, V. & KULČAR, Ž. (1984) Registar psihotika kao instrument evaluacije dijagnosticiranja schizofrenije. In *Psihijatrija* (ed. T. Baković), Zbornik radova VII kongresa psihijatara Jugoslavije, pp. 550–554. Budva: Udruženje psihijatara Jugoslavije.

FOLNEGOVIĆ-ŠMALC, V. (1979) Uloga bračnog stanja u toku schizofrenog oboljenja. *Socijalna psihijatrija*, 3, 233–319.

——, FOLNEGOVIĆ, Z., KULČAR, Ž., et al (1980) Nehospitalizirani shizofreni bolesnici u SR Hrvatskoj. In *Psihijatrija* (eds D. Kecmanović & S. Loga), VI kongres neurologa i psihijatara Jugloslavije, pp. 169–170. Sarajevo: Udruženje neurologa i psihijatara Jugoslavije.

FREEDMAN, A. M., KAPLAN, H. I. & SADOCK, B. J. (1980) *Modern Synopsis of Psychiatry*, Vol. II. Baltimore: Williams & Wilkins.

GIEL, R., SAUER, H. C., SLOFF, C. J. et al (1980) Epidemiological observations and schizophrenia and disability in the Netherlands. *Tijdschrift voor Psychiatrie*, 710–722.

GLASER, J. (1934) Tötungsdelikt als symptom beginnender oder schleichend verlaufender schizophrenie. *Zeitschrift für die gesammte Neurologie und Psychiatrie, Sonderabdruck*, 150, 1–41.

GULBINAT, W. & HENDERSON, J. H. (1986) Preface. In *Psychiatric Case Registers in Public Health* (eds G. H. M. M. ten Horn, R. Giel, W. H. Gulbinat, et al), pp. 1–10. Amsterdam: Elsevier Science Publishers.

HAILEY, A. M., HURRY, L. J., POWELL, M. et al (1974) Psychiatric services in Camberwell and Salford: statistics from the Camberwell and Salford register: 1964–1973. London: MRC Social Psychiatric Unit.

HARE, E. H. (1974) The changing content of psychiatric illness. *Journal of Psychosomatic Research*, 18, 283–289.

HAFNER, H. & AN DER HEIDEN, W. (1986) The Mannheim case register: the long stay population. In *Psychiatric Case Registers in Public Health* (eds G. H. M. M. ten Horn, R. Giel, W. H. Gulbinat, et al), pp. 28–38. Amsterdam: Elsevier Science Publishers.

HELGASON, L. (1977) Psychiatric services and mental illness in Iceland. *Acta Psychiatrica Scandinavica* (suppl. 268).

JENNINGS, C. (1985) *The Use of Psychiatric Case Registers in Public Health. Report of a WHO Working Group*. Groningen: WHO Collaborating Centre, Department of Social Psychiatry.

—— (1986) Inter register collaboration: the UK experience. In *Psychiatric Case Registers in Public Health* (eds G. H. M. M. ten Horn, R. Giel, W. H. Gulbinat, et al), pp. 14–25. Amsterdam: Elsevier Science Publishers.

KALIČANIN, P. (1975) *Primena Epidemiolškog Metoda Psihijatriji – Epidemiološki Aspekti Shizofrenije u Beogradu*. Belgrade: Institut za stručno usavršavanje i specijalizaciju zdravstvenih radnika.
—— (1987) Primena epidemiloškog metoda u proučavanju shizofrenije. *Engrami*, **1-2**, 215–221.
KESIĆ, B., KULČAR, Ž. & LEMKAU, P. V. (1981) Epidemiology of psychoses in Croatia, *Rad*, 392. Zagreb: Jugoslavenska Akademija Znanosti i Umjetnosti.
KULČAR, Ž., FOLNEGOVIĆ-ŠMALC, V., FOLNEGOVIĆ, Z., *et al* (1983) *Use of Computerized Case Registers in Follow-up Studies. Final Report PL 480-02-280 A*. Zagreb: Institute of Public Health of Croatia.
MUNK-JØRGENSEN, P. (1985) The schizophrenia diagnosis in Denmark. A register-based investigation. *Acta Psychiatrica Scandinavica*, **72**, 266–273.
—— (1987) Why has the incidence of schizophrenia in Danish psychiatric institutions decreased since 1970? *Acta Psychiatrica Scandinavica*, **75**, 62–68.
ØDEGAARD, Ø. (1952) The incidence of mental diseases as measured by census investigations versus admission statistics. *Psychiatric Quarterly*, **26**, 212–218.
SARTORIUS, N., JABLENSKY, A., KORTEN, A., *et al* (1986) Early manifestations and first-contact incidence of schizophrenia in different cultures. A preliminary report on the initial evaluation phase of the WHO collaborative study on determinants of outcome of severe mental disorders. *Psychological Medicine*, **16**, 909–928.
—— (1988) International perspectives of psychiatric classification. *British Journal of Psychiatry*, **152** (suppl. 1), 9–14.

STRÖMGREN, E. (1987) Changes in the incidence of schizophrenia? *British Journal of Psychiatry*, **150**, 1–7.
ten HORN, G. H. M. M. (1983) *Psychiatric Case Registers. Report of a Working Group. Mannheim, May 1983*. Copenhagen: WHO.
—— (1986) Definitions and classifications: introduction. In *Psychiatric Case Registers in Public Health* (eds G. H. M. M. ten Horn, R. Giel, W. H. Gulbinat, *et al*), pp. 170–174. Amsterdam: Elsevier Science Publishers.
WEEKE, A., MUNK-JØRGENSEN, P., STRÖMGREN, E., *et al* (1986) Changes in utilization of Danish psychiatric institutions I. An outline of the period 1957–1982. *Comprehensive Psychiatry*, **27**, 407–415.
WING, J. K., COOPER, J. E. & SARTORIUS, N. (1974) *The Descriptions and Classification Psychiatric Symptoms: An Instruction Manual of the PSE and CATEGO System*. London: Cambridge University Press.
—— (1986) Epidemiological research using psychiatric case registers. In *Psychiatric Case Registers in Public Health* (eds. G. H. M. M. ten Horn, R. Giel, W. H. Gulbinat, *et al*), pp. 14–25. Amsterdam: Eslevier Science Publishers.
WORLD HEALTH ORGANIZATION (1967) *Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death* (8th edn) (ICD-8). Geneva: WHO.
—— (1973) *The International Pilot Study of Schizophrenia*. Geneva: WHO.
—— (1984) *Uses of Epidemiology in the Study of the Elderly*. Technical Report Series, no. 706, Geneva: WHO.
—— (1988) *WHO Psychiatric Disability Assessment Schedule (WHO/DAS) With a Guide to Its Use*. Geneva: WHO.

*Vera Folnegović-Šmalc, MD, MSc, DSc, *Professor of Psychiatry, Head, Department of Psychiatry, Vrapče University Psychiatric Hospital, Zagreb, Yugoslavia*; Zdenko Folnegović, *Statistician, Head, Statistical Analysis and Computerised Processing Unit, Chronic Disease Service, Epidemiology Department, Institute of Public Health of SR Croatia, Zagreb, Yugoslavia*; Živko Kulčar, MD, DSc, *Professor of Epidemiology, Head, Chronic Disease Service, Epidemiology Department, Institute of Public Health of SR Croatia, Zagreb, Yugoslavia*

*Correspondence: *Klinička psihijatrijska bolnica Vrapče, 41090 Zagreb, Yugoslavia*