Chapter 3  Incidence in different geographical areas

One of the chief aims of the study was to collect series of cases of recent inception, which would allow an estimation to be made of the rates of incidence of schizophrenic disorders in the different catchment areas. In contrast to the large number of psychopathological, course and outcome, diagnostic, treatment, and family genetic studies, there have been relatively few large-scale epidemiological investigations on schizophrenia, and only a handful of them have addressed the issue of incidence. An overview of the design and methods of a selection of such studies in given in Table 1.1.

An essential step in the epidemiological study of any disease is the determination of the frequency of its occurrence in the two sexes and in different age groups, of the geographical variation in its frequency, and of its associations with other disorders and environmental factors. Incidence, i.e. the number of new cases occurring in a given population over a specified period per 1000, 10,000, or 100,000 persons at risk, is a particularly valuable index in the study of schizophrenia. Incidence rates are better suited than prevalence rates for comparisons between different populations, because they are less affected by differential mortality, migration, and other demographic factors. The study of series of patients of recent onset is important also in view of the possibility that pathogenetic or triggering factors which are active in the period preceding the first manifestations of the disorder may cease to operate at later stages of its evolution. Age- and sex-specific incidence rates, in comparison to prevalence rates, offer a better basis for the estimation of morbid risk (or disease expectancy), an index expressing the probability of developing a disease, provided that a given individual survives until a specified age.

METHODS OF ESTIMATION OF INCIDENCE AND MORBID RISK

The screening and case finding procedures employed in the field research centres, and the steps taken to ensure that no great numbers of eligible cases are missed, are described in chapter 1 of this report. Chapter 2 contains an analysis of the sociodemographic, clinical and diagnostic features of the included cases and outlines the rationale for presenting the data both in terms of a ‘broad’ diagnostic definition (CATEGO classes S, P, and O, or one of the above mentioned ICD clinical diagnoses), and in terms of a more specific and restrictive criterion, CATEGO class S-+.

In determining incidence, another two groupings were added to these alternative case definitions: (i) the cases falling into classes S, P, or O only, excluding patients who had a CATEGO class different from these, regardless of the clinical diagnosis; and (ii) the cases falling into classes S, P, or O+ only, excluding the O? class which may be assigned to ‘borderline’ or doubtful clinical pictures 1. Separate rates were calculated for these four levels of clinical and diagnostic specificity.

As pointed out in chapter 1, the analysis of incidence is based on data from the eight catchment areas in which fairly complete coverage was achieved of the various ‘helping agencies’ that were likely to serve as first-contact sites for psychotic patients. In six of these areas it was possible to explore, after the end of data collection, whether any ‘leakage’ of potential cases had occurred (see Table 1.5). The results of this additional enquiry indicated that few eligible patients had been missed. In the other two areas, a retrospective search for missed cases has not taken place, but, following site visits during which Headquarters and centre investigators reviewed in detail the case finding procedures, it was considered unlikely that a significant number of patients would have remained there undetected.

The data from the remaining five areas, in which the case finding was not complete, or where doubts existed about the population bases, were also treated as rates for the purpose of comparison. Because of the incomplete coverage, these rates were expected to be lower than the
The population data which provided the denominator values were taken from the census data for the year that was closest to the period of case finding in each centre. This corresponded to the 1980 round of censuses in most of the centres, for which detailed age- and sex-distributions of small areas had yet to be published. The denominator values used in the present publication were therefore usually provided directly by the appropriate national census office which performed any necessary extrapolations or estimations to cover the period of case-finding in each centre. For those centres which were surveyed prior to the publication, the denominator values were used in the present publication.

The morbid risk was estimated by the formula for an approximation of the accumulated incidence rate, CIR:

\[ \sum_{i} i_{t} \]

The summation from age group 1 to age group \( n \) of \( i_{t} \), where \( i_{t} \) is the annual incidence of age group \( t \) and \( t \) is the span of years included in age group \( t \), e.g. 5 for 5-year age-groups. This formula is applicable for cumulated incidence rates about or below 0.1. It is assumed that the age-specific incidence rates are constant over time, the morbidity risk of a condition may be approximated by the sum of rates for each age, i.e.:

\[ f_{t} = \text{annual incidence for females aged 15-19} \]
\[ m_{y} = \text{annual incidence for males aged 15-19} \]
\[ f_{t} = \text{annual incidence for females aged 20-24} \]
\[ m_{y} = \text{annual incidence for males aged 20-24} \]
\[ f_{t} = \text{annual incidence for females aged 25-34} \]
\[ m_{y} = \text{annual incidence for males aged 25-34} \]
\[ f_{t} = \text{annual incidence for females aged 35-44} \]
\[ m_{y} = \text{annual incidence for males aged 35-44} \]
\[ f_{t} = \text{annual incidence for females aged 45-54} \]
\[ m_{y} = \text{annual incidence for males aged 45-54} \]

then the morbidity rate for females is:

\[ 5(f_{1} + f_{2} + \ldots + f_{10}) \]

and for males:

\[ 5(m_{1} + m_{2} + \ldots + m_{10}) \]

**Effectiveness of the case-finding methods**

A question which arises in connection with the distributions is to what extent could the method of case-finding employed in this study result in a valid approximation of the ‘true’ incidence of schizophrenia and related disorders.

Deciding what constitutes the ‘true’ incidence of schizophrenia is bound to involve a good deal of arbitrariness, unless a pathophysiological marker of disease onset is available. In the absence of such a marker, the ascertainment of onset on the basis of clinical history will be unreliable in a substantial proportion of cases in which the early manifestations of the disorder represent a gradual accumulation of long-standing impairments or risk-related personality traits. A prospective monitoring of ‘true’ onsets is hardly ever feasible in epidemiological research. Most studies up to date have instead relied on the ‘social onset’ (Ödegård, 1946) of the disorder, which is defined by an event, such as a first admission.

The case-finding methods used in previous research fall into four broad groups: (i) the so-called genealogical random sample method (genealogischer Stichprobenent), introduced by Ritd (1916), which requires the collection of psychiatric morbidity data on the biological relatives of a random sample of ‘propo’s’ and allows the estimation of morbidity from prevalence data, assuming that onsets can be dated retrospectively, or involves a re-examination of the same population after some time during which a number of new cases have become manifest; and (ii) the birth cohort method (Klemperer, 1933; Fremming, 1947; Helgason, 1964) which presupposes the successful tracing and diagnosing of a sufficient large percentage of the members of the cohort, once they have passed through the entire period of risk, (iii) the population survey or census method (Brugger, 1931, 1933; Strömgren, 1938; Sjögren, 1948, etc.), which can produce incidence estimates from prevalence data, assuming that onsets can be dated retrospectively, or involves a re-examination of the same population after some time during which a number of new cases have become manifest; and (iv) the first admission method (Ödegård, 1946),

which depends on the monitoring and registration of hospitalizations, assuming that few cases fail to pass through the door of the psychiatric hospital. Each of these methods has advantages and inherent limitations; none was considered fully adequate for a cross-cultural comparative study.

The method of first-in-lifetime contact, employed in this study, is a close to the first admission method and represents an extension of this technique to non-hospital facilities and services which are rarely monitored in psychiatric epidemiology (e.g. the practitioners of traditional medicine, religious healers, and various social agencies). It is conceptually similar to the first ‘ever contact’ method of determining disease inception described by Wing & Fryers (1976) as part of the techniques used in psychiatric register studies. As applied in the Outcome study, the first-in-lifetime contact method does not eliminate the possibility that some schizophrenics may never make contact with any service and would therefore be missed. However, the relationship between such cases and patients who seek treatment would not vary widely across the different study areas.

This assumption may appear questionable, especially when areas with different density of services and different cultural patterns are being compared. There is no direct method for its verification, short of a door-to-door search and counting of cases who have never made a contact.

Nevertheless, some attempts at verifying this assumption were made in this study during the so-called ‘leakage surveys’, which were small-scale enquiries about missed cases, carried out with community agencies (such as private medical practitioners, hostels and shelters for the homeless, etc.) that had not been part of the original case-finding network. Although the priming goal of such enquiries was the identification of cases who actually had made a contact but were missed by the project team, key informants were also asked whether they knew about any other similar cases in the area. Except for the rural area of Chandigarh, where a small number of the study cases were identified by key informants in the community and the first contact with them was initiated by the project psychiatrist, hardly any symptomatically manifest cases who had not previously sought help could be found in the other areas. Thus, although no strict test could be given to the proposition that few psychotic patients remain ‘invisible’ to the helping agencies in a community, no evidence to the contrary was produced by the ‘leakage’ surveys.

A second, indirect way of estimating the magnitude of the ‘hidden morbidity’ problem is provided by the estimation of the proportions of the length of illness in the series of included cases. If in a given area the threshold for seeking treatment is much higher than in another area, one would expect to find in the former that the mean intervals between the time of onset of symptoms and the first contact with a helping agency are longer. As pointed out in chapter 2, there were no differences whatsoever between the developing countries and the developed countries as regards the proportions of patients who made a contact with a helping agency within six months of the onset of symptoms and those who made a contact after six months. In all the areas for which incidence rates are estimated (except Chandigargh, rural area, and Dublin), small percentages of cases could be found in which the first contact had been delayed by two years or more after the onset of symptoms. These percentages ranged from 3% in Aarhus to 10% in Nagasaki, but no centre had an excess of such cases. The data, therefore, do not indicate any marked differences between the study areas in respect of referral thresholds.

This conclusion finds further support in the observation (see chapter 2) that the reasons and events which lead to the index referral in schizophrenia are very similar across the centres. Therefore, Ödegård’s (1952) contention that most schizophrenics in the community eventually make a contact with aservice does not seem to be contradicted (at least as regards predominantly urban areas), and there is no reason to suppose that in any of the study settings the incidence rates reported here represent only a fraction of an ‘iceberg’ of hidden schizophrenic morbidity.

**MAIN FINDINGS ABOUT INCIDENCE**

**Annual incidence rates for age 15-54**

The one-year rates, calculated per 10000 population at risk in all the age groups between 15
The further inclusion of the CATEGO class O+ with borderline and dubious cases mainly diagnosed clinically as acute schizophrenic episodes or as unspecified subtype of schizophrenia, increased considerably the variation particularly because of a steep rise of the rates in the Chandigarh rural sample whereas the other rates varied by a factor of 2 to 5; only.

Further broadening the definition by including patients with a clinical diagnosis of schizophrenia and supposedly related disorders, but with other or no CATEGO classifications, the rates and variations between centres further increased, again with highest rates in the developing centre samples from Chandigarh rural and urban areas and the lowest rates in the Aarhus and Honolulu centres. The variation is two- and three-fold compared to the Chandigarh samples but less than two-fold when compared to centres in developed countries except for females in the Moscow centre which already by the SPO+ level showed an unexplained high rate of incidence.

The variation observed for the two broadest levels of definition is not surprising when considering the possible variability in incidence of various schizophrenia related disorders with more or less symptomatological resemblance or of borderline or dubious character. The variation is lower for the most restrictive definition by the S+ CATEGO class which is an indicator of symptomatically more severe and florid schizophrenia. Although the numbers of patients so defined are smaller the lower variation observed is not merely explained by decreasing the statistical power of analysis. When the mean rate also decreases even small fluctuations due to chance, for instance by missing or erroneous inclusion of a few cases will tend to cause a higher variation. This however did not occur, indicating that the S+ CATEGO class presents a robust syndromatical representation of schizophrenic conditions that may be detected reliably in various study areas and seems to occur with about the same frequency.

**Age- and sex-specific rates**

The age- and sex-specific rates for the CATEGO-SPO definition of schizophrenia and for the CATEGO S+ class definitions, are presented graphically in Fig. 3.2. The sex-specific rates are presented in tabular form in Table 3.1.
For the narrow S+ definition rates show marked peaks for males in five centres, one in age group 15–19 and four in age group 20–24; for females in four centres, one in age group 30–34 and two in age group 45–49. For the broad SPO definition male rates show marked peaks in the same age groups in the same five centres and in one further centre a peak appeared in age group 15–19. Female rates lost their peak patterns except for the two centres with peaks in age group 20–24. The pattern of age- and sex-specific rates thus showed a tendency to earlier onset in males than in females, a tendency which is further illustrated by Fig. 3.3 which shows the cumulative curves of onset in males and females in developed countries and in developing countries respectively. It suggests that women ‘consume’ their risk of developing a schizophrenic illness at a slower and more even rate than men, and that this pattern holds for both types of setting.

Considering the sensitivity of age- and sex-specific rates to small changes in sample composition, the emergence of a consistent pattern showing a sex difference, i.e. a later manifestation of schizophrenia in females in culturally and demographically different areas of the world represents an important finding. Apart from its significance in relation to genetic and clinical research in schizophrenia, it supports the validity of the diagnostic definition of the disorders included in this study by demonstrating their
cross-cultural similarity on such key parameters.

Since the age- and sex-specific manifestation rates of schizophrenic disorders are considered to be of particular importance from a geneticist’s point of view (Gottesman & Shields, 1982), the relevant findings for each study area are summarized below.

**Aarhus**
The ‘broad’ category of schizophrenia and related disorders shows a marked preponderance of males in the age groups 20–29, and a slight excess of females after the age of 30. The incidence in males shows a clear peak in the age group 20–24, while the less prominent peak of incidence is observed in females of the same age group. In the CATEG 5 category, the pattern is almost the same, except that no excess of female cases aged 30+ is observed. The shape of the curve of age-specific incidence of the S+ cases is very similar to that of the ‘broad’ diagnostic group.

**Chandigarh (rural area)**
In the ‘broad’ diagnostic category there is no clear-cut gender-related pattern, and no age-specific peak of incidence can be identified. In the S+ category, the number of males exceeds that of females in all age groups up to 34. There is, however, a clustering of female cases in the age group 40–49. The absence of a consistent age- and sex-related pattern may be due, in part, to the relatively small number of cases in this rural area, with relatively low numbers of population in the older age groups.

**Chandigarh (urban area)**
There is an excess of males in age groups 20–24 and of females in age group 35–44 in the ‘broad’ diagnostic group. There is a marked peak of incidence in the age group 20–24 in males but not in females. In the S+ group, males predominate in the age range 20–24 but have somewhat lower rates than females in the other age groups. The peak of incidence in males is in the 20–24 age group.

**Dublin**
In the ‘broad’ diagnostic category, there is an excess of males in the age groups 25–29 and 35–39 (but not in the age group 20–24 where the two sexes are equally represented, or in age group 45–49 where females predominate). In the S+ category, males exceed females in the age groups 15–29 and 35–39, while females exceed males in the age group 45–49. In females, a peak can be observed in the age range 45–49, for S+ cases only.

**Honolulu**
There is a marked excess of males in age group 20–24, and an excess of females after the age of 29, for both diagnostic categories. The peak of incidence is in the age 20–24 for males; and no clear-cut peak is found in the female population.

**Moscow**
At the level of the ‘broad’ diagnostic definition, there is an excess of males in the age group 18–19 only; the rates are similar for the two sexes in ages 20–39, and females are markedly overrepresented after the age of 40. There is a peak of incidence in males in the age 18–19, for females in the age group 30–34.

**Nagasaki**
In both the ‘broad’ diagnostic category and the S+ category, there is an excess of males in age groups 15–19 and 25–29: the two sexes show similar rates in other age groups. There is a peak of incidence in males aged 15–19 and in females aged 20–24. The shapes of the curves of the age-specific incidence of the ‘broad’ definition group and of the S+ group are very similar.

**Nottingham**
In both diagnostic categories there is a marked excess of males in the age groups 20–29, and some excess of females in the age groups 40–49. There is a peak of incidence in males in the age group 20–24 but no comparable peak in females. The shapes of the two distributions are very similar.

The overall impression is that the centres show similar patterns except for the Chandigarh rural and Moscow centres. In mos centres the rates tended to be higher in the younger age groups particularly for males, whereas the Chandigarh rural and Moscow centres had high rates in the older age groups and also showed high variations among age groups for SPO defined rates.
Morbidity risk

The expectancies of developing a disorder, for males and females passing through the entire period of risk between 15 and 54 years of age, are given in Table 3.2. For the ‘broad’ diagnostic category, the probability of developing the disorder varies from 0.50% in Honolulu to 1.72% in Chandigarh (rural area), and for the CATEGO S+ category from 0.26% in Honolulu to 0.54% in Nottingham.

Comparisons of the Results with Previous Data

Having established that the incidence rates and morbidity risk estimates reported in this study can be accepted as valid with a fair amount of confidence, it is important to examine the extent to which they confirm or contradict previously reported epidemiological data.

In Aarhus, both the rate for the ‘broad’ group of schizophrenia and related disorders and the rate for CATEGO S+ cases, appear to be higher than the Danish average first admission rate for schizophrenia (0.51 per 10000) for the period 1970-9, calculated on the basis of the national psychiatric case register (Joensen & Wang, 1983). Nielsen (1976) calculated the ‘first-time referral’ rate for schizophrenia (excluding reactive psychoses) on the island of Samsø near Aarhus to be 20 per 10000. A direct comparison, however, could be misleading because the Outcome study category of ‘broadly’ defined schizophrenia includes a proportion of cases with centre diagnosis of reactive paranoid psychosis. In the national statistics of Denmark, all reactive psychoses (ICD 298, which includes also those with predominantly affective or confusional features) are reported separately, and show a rate higher than schizophrenia (3.2 per 10000). A recent analysis of the national case register data over the period 1970-84 (Munk-Jørgensen, 1986) indicated a trend of decreasing first-admission rates for the diagnosis of schizophrenia accompanied by a significant increase in the frequency of diagnoses such as paranoid and unspecified psychoses, or ‘borderline states’. Compared with other Scandinavian studies, the Aarhus rates for ‘broad’ schizophrenia, as defined by the Outcome study criteria, do not appear to be very different.

Most Scandinavian studies have produced estimates of morbidity risk, using different methods but taking advantage of the demographic stability of the population and of the exhaustive versus case register data. Using the census method, Strömgren (1938) estimated the risk for schizophrenia (both sexes) at 0.47% for the island of Bornholm, a figure very close to the estimate 0.56% for ‘broad’ schizophrenia in the Aarhus area in this study. Other Scandinavian studies quoted in Table 3.3. In this connection, it should be noted that morbidity risk figures for schizophrenia in European populations appear to be not only similar but also remarkably stable over time. On the basis of data from 18 German, Swiss, and Scandinavian studies conducted in the 1920s and 1930s, Strömgren (1950) derived a lifetime risk estimate of 0.72% for men and
women combined. The risk estimates for the European centres in this study (0.99% in Aarhus, 0.83% in Dublin, 1.13% in Moscow, and 0.80% in Nottingham) are of the same order of magnitude.

The rates in Chandigarh cannot be compared with analogous Indian data, because practically all previous epidemiological studies of schizophrenia on the Indian subcontinent (reviewed by Wig, 1982) have been prevalence surveys. These surveys have produced prevalence rates for psychosis of the order 5-10 per 1000 population, which is comparable to prevalence rates in European and North American populations. First admission data on schizophrenia are, however, available for the Indian population in Mauritius (Murphy & Raman, 1971; Raman & Murphy, 1972). For the year 1956, the total rate in age groups 15-44 was 1 per 10000 (Hindi Indians) and 0.9 per 10000 (Moslem Indians). Much higher rates, especially in women aged 35-44, were found in Indians living in Singapore (Kadri, 1965; Murphy, 1968). In spite of the differences in methods and settings, these data do not conflict with the Chandigarh findings, which also suggest a rather high rate in females after the age of 35.

The Dublin data are of special interest, in view of previous findings of unusually high prevalence (Walsh et al, 1980; Terry et al, 1984) and first admission rates for schizophrenia (5.7 per 10000 in males and 4.6 per 10000 in females - Walsh, 1969). These survey findings are in accordance with national first admission data (4.5 per 10000 for the two sexes and all ages in 1978 - O'Hare & Walsh, 1980) and at variance with the data for Northern Ireland (Murphy & Vega, 1982) where the first admission rates are of the order of 1.6 to 3.7 per 10000, i.e. very similar to the first-contact rate for Dublin reported here. Although the allegedly high Irish incidence rates have led to interesting speculation about possible underlying factors (Torrey, 1980), it seems that a large part of the explanation may be found in the overestimation of the number of first admissions by hospitals, a practice common to many reporting systems. Since the establishment of three case registers in Ireland (Blake et al, 1984), which ensured the accurate enumeration of first-contact patients at the psychiatric services, the rates for schizophrenia no longer appear to be higher than elsewhere. The incidence rates found in a survey in three Irish counties in the present study (using the principal clinical instrument of the Nuaillain et al, 1984) agree quite well with the rates established in the present study, although the possibility cannot be ruled out that in some rural areas in the western part of Ireland true pockets of high rate of schizophrenia may exist.

No incidence or first admission rates, produced by earlier research, are available for Honolulu but psychiatric case register data (Weiner & Marvit, 1977) suggest that the prevalence of schizophrenia among Caucasians in Hawaii is the same as in mainland US (it is somewhat higher in other ethnic groups in Hawaii). Most of the US epidemiological studies (reviewed by Babigian, 1980) have reported treated incidence rates for the population aged 15+ in the range of 30 to 120 per 10000. The Monroe county case register (Kramer, 1980) has produced the figure 6.8 per 10000 but only one half of these first admissions were actually first-in-lifetime hospitalizations and, in addition, some of the patients had had earlier spells of out-patient treatment. The older US rates have also been affected by the very broad definition of schizophrenia prior to the introduction of DSM-III. According to Babigian, the application of DSM-III criteria to the Monroe county data would result in a further reduction of the rate by 20-30%, and would bring it down to about 20 per 10000, which would be close to the Honolulu rate in this study.

Previous epidemiological studies in Moscow (Liebermann, 1974; Shmaonov, 1983) indicate an incidence rate of schizophrenia of 1.91 per 10000 (1.98 in males and 1.85 in females). The figures are based on a census of all patients registered by the psychiatric dispansary and a retrospective dating of onsets. These rates are somewhat lower than the first-contact rates found in the present study. Closer to the latter are the first admission rates for schizophrenia (2.3 per 10000) reported by Krasik & Semyon (1980) for the city of Tomsk in Western Siberia. All previously reported Soviet rates show peaks of incidence in young males (up to age 19) and in middle-aged females.

The Nagasaki rates in this study cannot be compared with other Japanese data because previous surveys in that country have been almost exclusively prevalence-oriented (Kato, 1969; Torrey, 1980). The latter have shown a fairly stable average national prevalence of 2.3 per 10000, although considerable regional variations have been described. Morbid risk for schizophrenia has been estimated on the basis of at least 15 prevalence surveys carried out between 1940 (Nakane et al, in press). The risk estimates have varied from 0.48 to 2.47%, with a median value of 0.82%.

The Munich data should be compared with what comes closest to the case definition in the present study - namely, the 'first-ever contact' rate for patients entering the psychiatric registers in Camberwell (London) and Salford (Wing & Fryers, 1976). These rates were of similar size in Camberwell (total rate 1.4 per 10000; 1.4 for males and 1.5 for females) and somewhat lower in Salford (total rate 1.1 per 10000; 1.2 for males and 1.0 for females).

The above overview shows that the first-contact incidence rates and morbid rates, particularly for the 'broad' definition of schizophrenia and related disorders established in the present study, correspond well to previous findings or estimates of the frequency of these conditions in the individual study areas or countries. By applying a uniform case definition and case finding methodology, as well as standardized tools for the clinical description of the patient populations in the different settings, the study has shown that no large difference is seen in the manifestation rate of schizophrenic disorders across cultures and geographical areas that are as wide apart as Denmark and India, or Japan. This, of course, does not exclude the possibility that pockets of unusually high or unusually low incidence may be found in different populations (e.g. the morbid risk of 2.66% calculated by Boek, 1980, and Boek et al, 1978, in a population isolate in northern Sweden). The reasons for such deviations are far from being well understood, but it is increasingly clear that they represent exceptions rather than the rule in the global epidemiological pattern of schizophrenia.