Part I

The social epidemiology of schizophrenia
Introduction

Social epidemiology studies the link between the social environment and the development and distribution of diseases in populations (Kaufman and Cooper, 1999). Research into social and behavioural determinants of health and illness is an area of interest for both sociologists and social epidemiologists. This section provides an introduction to some design and conceptual issues in social epidemiology and detailed discussion of temporal and geographical variations in the incidence, course and outcome of schizophrenia, with particular emphasis on issues of urbanization and migration.

Epidemiologists are very familiar with individual-level effects or risk factors such as birth complications, smoking or substance misuse. However Bresnahan and Susser in Chapter 1 emphasize the importance of societal-level effects (such as racism or level of socioeconomic development) in elucidating disease trends and mechanisms. The use of age–period–cohort effect analyses and life-course approaches to epidemiology are also included.

One of the central tenets of schizophrenia epidemiology is that the (narrowly defined) disorder appears to occur with equal incidence worldwide. However some variation in incidence rates between the developed and developing world has been noted for broadly defined schizophrenia. Bresnahan and colleagues examine this issue in Chapter 2 but recognize that the question of variation in incidence will remain unresolved ‘while we await incidence rates based on rediagnosis using modern diagnostic systems’. On the other hand, there is ‘clear and convincing evidence’ currently available for more favourable course and outcome of schizophrenia in developing countries. This finding is ‘remarkable’ in view of the scarcity of treatment options in the developing world. Bresnahan and colleagues conclude that some aspect of the cultural circumstances in developing countries may provide a more therapeutic context for recovery.

Is schizophrenia disappearing? In Chapter 3 Bresnahan and colleagues investigate whether the incidence of schizophrenia has been declining over the past few decades. They consider that the apparent decline appears to reflect mainly period effects, pointing again to the role of social environment. Is schizophrenia becoming
less severe? Bresnahan and colleagues also examine time trends in course and outcome of schizophrenia and find that improvements in outcome from the beginning to the end of the 20th century are modest. As the authors point out, this is surprising in view of the dramatic impact of antipsychotic medication on symptoms. Unfortunately, the data used to detect changes in outcome are unsystematic and do not yield insight into possible explanatory factors.

In Chapter 4, Boydell and Murray examine urban birth and migration as risk factors for schizophrenia. They conclude that there is ‘substantial’ evidence that urban birth and/or upbringing are associated with an increased risk for psychosis and that this effect may be increasing. The high rate of schizophrenia and psychosis among migrant groups, particularly first- and second-generation African-Caribbean immigrants in the UK, has been the subject of much discussion and debate over the past few years. Boydell and Murray examine the many possible reasons why ‘urban birth’ and ‘migration’ may increase the incidence of schizophrenia. Although there are no clear answers at present, the authors conclude that social and psychological aetiological factors are likely to be important. It seems as though researchers into schizophrenia will have to pay more attention to the social environment in the future to help to solve these unanswered questions.

REFERENCE

Investigating socioenvironmental influences in schizophrenia: conceptual and design issues

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The investigation of socioenvironmental influences began early in the history of schizophrenia research. As far back as the 19th century, reports emerged that insanity was more common among the lower social classes, and early in the 20th century this association was reported specifically for the diagnosis of schizophrenia. The association between low social class and schizophrenia was later confirmed by the classic study of Hollingshead and Redlich in New Haven in the 1950s (Hollingshead and Redlich, 1958). They suggested that the relation was causal: lower social class increased the risk of schizophrenia. This view was shortly disputed, however, in another classic study by Goldberg and Morrison (1963). Relying upon national registry data to establish occupation of father at birth, Goldberg and Morrison found that fathers of patients had a social class distribution similar to the population as a whole. Despite decades of work and further exceptional contributions (Link et al., 1986; Dohrenwend et al., 1992; also see Table 1.1), the matter is still not entirely resolved; however, the weight of evidence suggests that socioeconomic status has at most a modest effect on risk of schizophrenia. Therefore, while social class provided an early foothold in the examination of socioenvironmental influences in schizophrenia, no clear findings have emerged.

Nonetheless, emanating from this initial concern with social class, researchers have extended investigations to a broad range of socioenvironmental influences in schizophrenia. This section addresses socioenvironmental influences that are an active focus of current research and appear to have an impact on schizophrenia. The chapters to follow deal in turn with socioeconomic development (Ch. 2), time trends (Ch. 3), and urbanicity and immigration (Ch. 4). What ties these together is that, in each domain, social environment is likely to be a significant contributing factor to any observed variation in schizophrenia morbidity. In addition, they represent societal influences that cause populations to differ from one another, but they may not account for differences between individuals within a given population.
Table 1.1. Social class of origin and risk of schizophrenia

<table>
<thead>
<tr>
<th>Study</th>
<th>Study description</th>
<th>Paternal social class</th>
<th>Diagnosis</th>
<th>Finding</th>
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</thead>
<tbody>
<tr>
<td>Goldberg &amp; Morrison (1963)</td>
<td>Psychiatric Register; first admission (1956)</td>
<td>Paternal occupation at birth General Register Office (I–V)</td>
<td>Register diagnosis</td>
<td>Social class distribution of fathers of patients at birth similar to that of the population as a whole</td>
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<td>England/Wales</td>
<td>Compared with population statistics</td>
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<td>Turner and Wagenfeld (1967)</td>
<td>Psychiatric Register, all first contact (1960–63) diagnosed with schizophrenia having no prior psychiatric hospitalization (n = 214)</td>
<td>Paternal occupational score (1–7) for last/current/usual job, and job when patient was 16</td>
<td>Register diagnosis</td>
<td>Paternal occupation when patient was 16 years and usual occupation over-represent the lowest prestige categories compared with expectation</td>
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<tr>
<td>Monroe County, New York</td>
<td>Compared with population statistics</td>
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<tr>
<td>Wiersma et al. (1983) the Netherlands</td>
<td>Incident treated cases (Schizophrenia n = 34) Compared with random sample of general population</td>
<td>Paternal status on occupational scale (1–5/6)</td>
<td>ICD-9 schizophrenia (295)</td>
<td>Paternal occupation tended to be higher than expected based on the population sample; the relationship was not linear</td>
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<tr>
<td>Castle et al. (1993) Camberwell, UK</td>
<td>Psychiatric Case Register (1965–84), first contact (n = 128) Matched nonpsychotic patients in the Register (n = 128)</td>
<td>Paternal occupation at birth medical records or Birth Record data, General Register Office (I–V). Occupations dichotomized (nonmanual/ manual)</td>
<td>RDC criteria, schizophrenia</td>
<td>Patients were twice as likely to have fathers in manual occupations than nonpsychotic matched psychiatric patient controls</td>
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<tr>
<td>Jones et al. (1994) UK</td>
<td>1946 British Birth Cohort (cases, n = 30; stratified random sample of cohort; n = 5362)</td>
<td>Paternal occupation at birth General Register Office (I–V)</td>
<td>DSM-III-R schizophrenia</td>
<td>Social class at birth not associated with later risk of schizophrenia; a nonsignificant trend towards higher social class increasing risk reported</td>
</tr>
<tr>
<td>Study</td>
<td>Year</td>
<td>Birth Cohort</td>
<td>Paternal Occupation at Birth</td>
<td>Social Class of Origin</td>
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<tr>
<td>Done et al. (1994)</td>
<td>1958</td>
<td>British Birth Cohort</td>
<td>General Register Office (I-V)</td>
<td>UK (cases, n=100; controls 10%)</td>
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<tr>
<td>Makikyro et al. (1997)</td>
<td>1966</td>
<td>Finnish Birth Cohort</td>
<td>Office (I–V)</td>
<td>Finland (cases, n=76; cohort =11017)</td>
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<tr>
<td>Timms (1998)</td>
<td>1963</td>
<td>Stockholm Cohort</td>
<td>Hospital admissions for classification used by National Stockholm County (1969-85); Central Bureau of Statistics (1-5) trichotomized</td>
<td>Sweden</td>
</tr>
</tbody>
</table>

Notes: Studies appearing in the table include incident cases of diagnosed schizophrenia, and individual measures of parental social class (occupation). Studies excluded from the table do not meet all three inclusion criteria. For example, Hollingshead and Redlich (1958) was not included because the measure of social class combined education and occupation and residence. Lapseau et al. (1956) not included because measure of class was based on residence. See text for diagnostic criteria.
Societal influences have rarely been addressed in recent reviews of schizophrenia epidemiology. Of course, neither societal nor individual social experience are considered as alternatives to biological causation; they are, however, often antecedent and account for patterns of biological exposures.

In order to appreciate and understand fully the range of epidemiological studies represented, it is helpful to be familiar with certain central concepts in the epidemiology. Epidemiological studies of socioenvironmental influences often address questions framed by contrasts (Schwartz and Carpenter, 1999). Why do some individuals in a population develop disease and not others? Why is the rate of disease higher/lower in one population compared with another? Why is the rate of disease changing over time? How does experience in each stage of life build on risk arising from earlier experience? These questions all fall squarely within one of the key missions of epidemiology: to identify determinants of disease. The strategies that can be used to answer each of these questions are quite different, however, and focus attention on distinct effects. As these differences are often overlooked and have important implications, we draw attention to them here.

**Effects at the level of the individual**

Why do some individuals develop schizophrenia and not others? This question pertains to individuals. To answer this question, we focus on variation between individuals in hypothesized risk factors. Thus, we establish both the exposure and disease experience for individuals under study within a given population, using such strategies as cohort and case-control studies. When there is evidence of association between exposure and disease, effort is directed at determining if the connection is causal (Schwartz and Susser, 2001).

In searching for determinants in this way, the natural focus is on factors that vary between individuals within the population at hand. For example, we hypothesize that prenatal exposure to influenza is a risk factor for schizophrenia. This hypothesis is testable in a population when some individuals are exposed and some are not. We then compare the proportion of those exposed to prenatal influenza who develop schizophrenia with the proportion of those not exposed to prenatal influenza who develop schizophrenia.

This much is well known to most schizophrenia researchers. There are two constraints to the approach, however, that are not widely recognized. First, when there is no interindividual variation in a factor, it cannot explain why some people within a population get disease and not others. A factor that is ubiquitous in a given population will not contribute to individual variation of risk in that population even if it can and does contribute to disease (Schwartz and Carpenter, 1999). For example, in an ethnically homogeneous population, there may be little variation between
individuals in skin complexion; therefore, complexion may not be identified as a determinant of individual risk for skin cancer within this population. Paradoxically, this could occur within a population consisting wholly of individuals whose complexion puts them at extremely high risk (e.g. a Nordic population). A number of individual factors that are of compelling interest in schizophrenia research may be ubiquitous within samples commonly studied (e.g. poverty, race), with the result that their effects are undetectable.

An intriguing example of an ubiquitous exposure are childhood vaccinations. In the field of psychiatry, interest in the impact of vaccines has surfaced in the context of childhood autism. Recently, hypotheses have been advanced relating the MMR (measles, mumps and rubella) vaccine to autism. Because this vaccination is ubiquitous in most developed countries, it is extremely difficult to examine the impact of vaccines on differences in risk for autism within one of these populations.

Second, the relationship of exposure to disease necessarily varies across populations. Because disease causation is multifactorial, whether or not a given factor causes disease will depend upon the presence of other factors (i.e. cofactors in disease causation). The presence of these other factors will clearly vary between populations. Consequently, there is no expectation that individual risk factors identified in studies of individual level effects will be exactly the same from population to population, nor is there an expectation that the magnitude of relative risk pertaining to the risk factor will be the same from population to population. For example, if prenatal influenza acts as a risk factor for schizophrenia only in conjunction with adverse postnatal exposures, the association of influenza and schizophrenia will be affected by the prevalence of these postnatal cofactors in the population. Despite this caveat, one generally does expect some consistency across studies in different populations, and the lack of it is a source of concern or interest.

Studies of individual risk factors for schizophrenia are vital, and in subsequent chapters we will see that they have made important contributions in schizophrenia research. It is equally important, however, to investigate the role of societal level factors in the causation of schizophrenia.

Effects at the societal level

Usually the investigation of societal effects begins with the question: Why is the rate of disease higher/lower in one population compared with another? This question contrasts populations rather than individuals within populations, focusing on differences in the rates of disease between populations. With the shift in focus from individual to societal level effects, the range of substantive questions has changed (Rose, 1992; Schwartz, 1994; Schwartz and Carpenter, 1999).

The critical contribution of contrasting populations, rather than individuals
within populations, is to draw attention to factors with meaning residing at the societal level. Contextual factors such as stage of socioeconomic development are defined at the societal level: individuals within a society share the experience of living in a ‘developed’ or ‘developing’ country. Similarly, average individual income in a society, although constructed from an individual factor, describes a milieu or societal characteristic: individuals living in the population share the experience of living in a low-income or high-income society. Societal racism (political, economic and social) is also definable at the group level. The association of societal measures of the degree of contextual racism with rates of schizophrenia in groups of minorities living in different societies may illuminate the impact of a broad group-level phenomenon. Investigations of differences between populations are particularly crucial to identifying and describing these sorts of factor as determinants of rates of disease.

Sometimes the distinction between an individual- and population-level factor is obvious; however, in other instances it is not. It is important to clarify the distinction or delineate levels in order to avoid mistaken inference. An example particularly germane to schizophrenia research is the impact of ‘treatment’. There is definitive evidence that within given populations modern treatments (e.g. medications, family interventions) reduce the risk of relapse in patients with schizophrenia. From this evidence, however, it cannot be inferred that a society with more highly developed treatment systems – even including the most effective treatments – will have lower rates of relapse among patients with schizophrenia. In fact, for reasons that remain unclear, the course of schizophrenia is substantially better in societies with the least developed treatment systems (Ch. 2). Some have speculated that treatment systems lead to segregation and enhanced stigma on a societal level, and that they interfere with reintegration. Therefore, ‘treatment’ has a different meaning at societal and individual levels. This distinction is often overlooked.

It is possible to conduct studies where both individual and societal level effects are examined at the same time. For example, in a multisite study conducted in several countries, it would be possible to consider both individual income and mean societal income/level of socioeconomic development in the same analysis. The impact of societal level factors on individual processes, and their interaction with individual level factors to affect individual processes, can be examined. With notable exceptions (van Os et al., 2000), there are still few examples of such analyses in schizophrenia research.

Sometimes studies contrast populations when seeking to identify individual effects. It is always risky to make comparisons at one level and inferences at another. Nonetheless, differences between populations can provide important indirect evidence for the impact of individual factors that do not vary within a given population. In the example described above, skin complexion was confined to a very
narrow range in a hypothetical population. A comparison of this population with
another ethnically dissimilar population may yield a comparison of two popu-
lations of wholly different complexion (e.g. Nordic versus Ugandan). This compari-
son might contribute important information about complexion as a determinant
of skin cancer. Migrants studies, most often used to isolate genetic from environ-
mental causes of disease, may also uncover the causal contribution of ubiquitous
environmental exposures. Systematic first- and second-generation differences
between rates in immigrant populations in the country of destination and popula-
tion rates in the country of origin provide nonspecific evidence for environmental
determinants. Higher rates of schizophrenia among African-Caribbean immi-
grants than found in countries of origin are consistent with a number of possible
mechanisms including discrimination stress, a potential ubiquitous exposure
among immigrants (Ch. 4). Unfortunately, migrant populations are not always
available for study.

Age–period–cohort effects

Why is the rate of disease increasing/decreasing within a population over time?
Contrasting the same population at different points in time is akin to comparing
different societies. Instead of comparing the rate in one society with that in another,
the rate of disease in the same society is being compared at one time with another.

In spite of the apparent similarities between these comparisons, there are impor-
tant differences. Dynamic socioenvironmental influences are the leading suspect as
a cause of secular trends. The time periods analysed are generally too brief to
capture significant shifts in population genetics. In comparisons between popula-
tions, however, population genetic differences are more likely to play a role along-
side socioenvironmental factors.

Another important distinction is in the analytic techniques. Time is continuous,
whereas populations are categorical. The differences over time are measured in
change. Moreover, change over time can be measured in three dimensions: histor-
ical period, age and cohort (usually birth cohort defined by year of birth). The view
of rate change is different in each of these metrics. Disentangling the three time
effects is essential for interpretation of secular trends; for understanding the liter-
ature on change in schizophrenia incidence, it is helpful to understand how these
dimensions are differentiated.

Period effects

Period effects capture the point-in-time experience of a population, i.e. specific his-
torical conditions such as an economic depression or war. Increased rates of suicide
during economic depression or decreased rates of suicide in wartime are examples