The Epidemiology of Schizophrenia

Edited by

Robin M. Murray
Institute of Psychiatry, London, UK

Peter B. Jones
University of Cambridge, UK

Ezra Susser
Columbia University and
New York Psychiatric Institute,
New York, USA

Jim van Os
University of Maastricht, the Netherlands

and

Mary Cannon
Institute of Psychiatry, London, UK

CAMBRIDGE
UNIVERSITY PRESS

PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE
The Pitt Building, Trumpington Street, Cambridge, United Kingdom

CAMBRIDGE UNIVERSITY PRESS
The Edinburgh Building, Cambridge CB2 2RU, UK
40 West 20th Street, New York, NY 10011-4211, USA
477 Williamstown Road, Port Melbourne, VIC 3207, Australia
Ruiz de Alarcón 13, 28014 Madrid, Spain
Dock House, The Waterfront, Cape Town 8001, South Africa

http://www.cambridge.org

First published 2003

Printed in the United Kingdom at the University Press, Cambridge

Typeface Minion 10.5/14pt *System* QuarkXPress™ [SE]

A catalogue record for this book is available from the British Library

Library of Congress Cataloguing in Publication data

The epidemiology of schizophrenia / editors Robin M. Murray . . . [et al.].
p. cm.
Includes bibliographical references and index.
ISBN 0 521 77540 X (hb.)
1. Schizophrenia – Epidemiology. I. Murray, Robin.

RC514 .E425 2002
362.2′6 – dc21 2002017390

ISBN 0 521 77540 X hardback

Contents

1

Investigating socioenvironmental influences in schizophrenia: conceptual and design issues

Michaeline Bresnahan and Ezra Susser

Division of Epidemiology, Columbia University, New York, USA

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.

Study	Study description	Paternal social class	Diagnosis	Finding
Goldberg & Morrison (1963) England/Wales	Psychiatric Register; first admission (1956) ($n=369$) Compared with population statistics	Paternal occupation at birth General Register Office (I–V) Comparison: 1931 Census of Occupied Men ages 20–44	Register diagnosis	Social class distribution of fathers of patients at birth similar to that of the population as a whole
Turner and Wagenfeld (1967) Monroe County, New York	Psychiatric Register, all first contact (1960–63) diagnosed with schizophrenia having no prior psychiatric hospitalization ($n=214$) Compared with population statistics	Paternal occupational score (1–7) for last/current/usual job, and job when patient was 16 Comparison: 1950 County Census occupations, age and sex adjusted	Register diagnosis	Paternal occupation when patient was 16 years and usual occupation over-represent the lowest prestige categories compared with expectation
Wiersma et al. (1983) the Netherlands	Incident treated cases (Schizophrenia $n=34$) Compared with random sample of general population	Paternal status on occupational scale (1–5/6)	ICD-9 schizophrenia (295)	Paternal occupation tended to be higher than expected based on the population sample; the relationship was not linear
Castle et al. (1993) Camberwell, UK	Camberwell Cumulative Psychiatric Case Register (1965–84), first contact ($n=128$) Matched nonpsychotic patients in the Register ($n=128$)	Paternal occupation at birth medical records or Birth Record data, General Register Office (I–V). Occupations dichotomized (nonmanual/manual)	RDC criteria, schizophrenia	Patients were twice as likely to have fathers in manual occupations than nonpsychotic matched psychiatric patient controls
Jones et al. (1994) UK	1946 British Birth Cohort (cases, $n=30$; stratified random sample of cohort; $n=5362$)	Paternal occupation at birth General Register Office (I–V)	DSM-III-R schizophrenia	Social class at birth not associated with later risk of schizophrenia; a nonsignificant trend towards higher social class increasing risk reported

Done et al. (1994) UK	1958 British Birth Cohort (cases, $n=40$; controls 10% of sample with no history of psychiatric admission)	Paternal occupation at birth General Register Office (I–V)	PSE, CATEGO	Social class of origin significantly higher for preschizophrenics than for controls
Makikyro et al. (1997) Finland	1966 Finnish Birth Cohort (cases, $n=76$; n cohort $=11017$)	Paternal occupation at birth (I–V)	DSM-III-R schizophrenia	Incidence of early-onset (<23 years) schizophrenia higher than expected in the highest social class (I) compared with lower social classes (II–V)
Timms (1998) Sweden	1963 Stockholm Cohort of residents born in 1953; cases ($n=71$) hospital admissions for Stockholm County (1969–83, i.e. cohort ages 16–30; n cohort $=15117$)	Parental occupation at member age 10 from population register; classification used by National Central Bureau of Statistics (1–5) trichotomized	ICD-8 schizophrenia Inpatient Register Diagnosis	Low parental social class at patient age 10 not related to risk of schizophrenia; middle-class parental status related to increased risk of schizophrenia compared with working class (nonsignificant)

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 occupation and residence; Lapouse 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 populations of wholly different complexion (e.g. Nordic versus Ugandan). This comparison might contribute important information about complexion as a determinant of skin cancer. Migrants studies, most often used to isolate genetic from environmental 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 population rates in the country of origin provide nonspecific evidence for environmental determinants. Higher rates of schizophrenia among African-Caribbean immigrants 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 important 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 populations, however, population genetic differences are more likely to play a role alongside 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: historical 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 literature 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 historical conditions such as an economic depression or war. Increased rates of suicide during economic depression or decreased rates of suicide in wartime are examples

of period effects. Similarly, a change in the diagnostic system in use during the period of measurement will be reflected as a period effect. Thus, the incidence rate of schizophrenia should be higher in years when a broader definition of disease is in use, and lower in years when a narrower definition of disease is in use (e.g. rates of schizophrenia in 1960 versus 1990). Secular trends attributable to artifact (i.e. changes in diagnostic criteria, changes in ascertainment) are often subsumed in period effects.

Age effects

Age effects reflect the varying susceptibility to disease over the life cycle. In schizophrenia, peak risk for onset occurs during young adulthood. Because age structures risk, the underlying age structure of a population will affect overall rates. A population that is 'younger' (i.e. where a greater proportion of individuals are in their young adult years) will be expected to have higher overall incidence rates than a population that is 'older' (i.e. where a greater proportion of individuals are in ages of lower risk of onset). In studies of schizophrenia trends, the principal reason for interest in age effects is based on their capacity to introduce artifact or confounding in trend analyses. When the age structure of the population changes, the overall population rates will change. Age stratification and age standardization are used to address these problems.

Generational effects

Generational effects or cohort effects capture the effect of cumulative experiences in population groups, usually defined by birth year. Trends based on the disease experience of birth cohorts reflect the unique group experience of being in utero in a given year, experiencing childhood during a given historical period and adulthood during a specific period. Therefore, the cumulative experience of people who are 30 years old in 1960 is different from people who are 30 years old in 1990. When this causes a difference in disease rates, it is a generational effect. If the investigator is interested in the impact of childhood exposures, individuals who are 30 years old in 1960 are the same as people who are 5 years old in 1935. When there is evidence of generational shifts in rates over short periods of time (measured in birth years), differences arising from fetal or infant experience are implicated.

Discriminating age–period–cohort effects

For interpretation of secular trends, it is essential to separate these component effects: period, age and cohort. This represents a first step to developing hypotheses and investigating the causes of the rate changes (Susser, 1973). It can be difficult, however, to disentangle these effects. Figures 1.1 and 1.2 are graphical displays that allow visual discrimination of these effects.

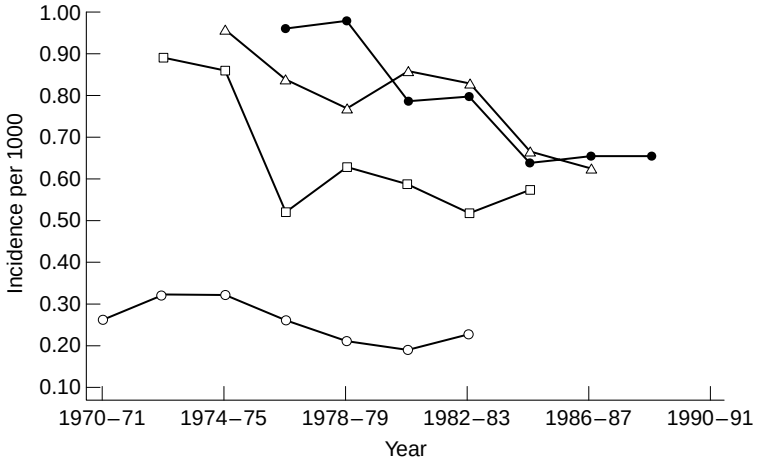

Fig. 1.1. This graph shows age-stratified incidence of schizophrenia by calendar year. These period data for four age groups (male aged 16–17 (○), 18–19 (□), 20–21 (△) and 22–23 (●) years) are taken from Suvisaari et al. (1999). The study followed individuals born from 1954 to 1965 over the period from 1970 to 1991 for schizophrenia. In this figure, we see a period effect with generally declining rates over time in all age groups except the 16–17 year olds, and age effects with ages 16–17 years at lowest risk and ages 20–21 and 22–23 years at highest risk.

Age–period confusion is common. For example, risk of drug use varies with age, adolescents and young adults being at highest risk. At the same time, the availability of illicit substances varies over historical period. A period effect owing to the increased availability of illicit drugs could be masked by a change in the age structure in the population. If adolescents and young adults decrease as a proportion of the population from one historical period to another, this will produce a countervailing trend towards reduced drug use. A comparison of historical period within age groups would expose the period effect.

Age–cohort confusion can also occur. For example, when a generation particularly inclined to drug use enters adolescence, it will at first appear that there is a high rate of drug use among adolescents. This would suggest an age effect. However, following this generation as they age will reveal their proclivity to drug use. As the generation grows older, they will have higher rates at every age than the preceding or subsequent generations examined at the same age. A comparison of birth years within age groups would expose the cohort effect.

Discriminating between period and generation effects can be illuminating in understanding disease processes. The classic example of a Gordian knot was posed by trends in tuberculosis mortality (Susser, 1973). As the rates of tuberculosis declined over time (1880 to 1930), a steady increase in risk with age was observed

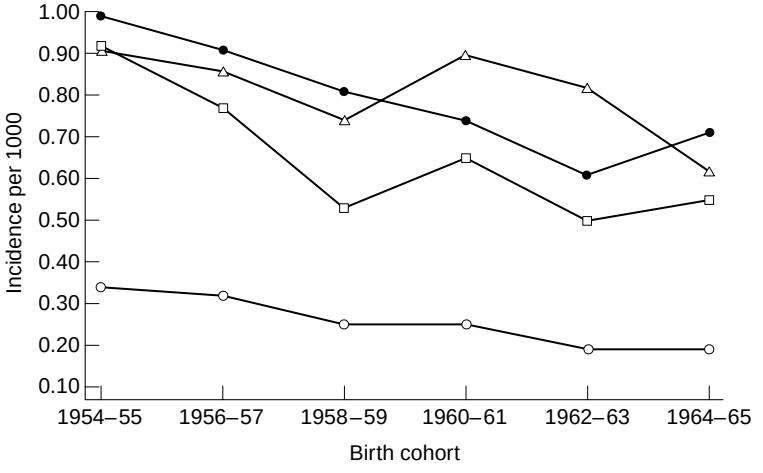

Fig. 1.2. This graph shows age-stratified incidence of schizophrenia by year of birth. The data for four age groups (males aged 16–17 (○), 18–19 (□), 20–21 (△) and 22–23 (●) years) are taken from Suvisaari et al. (1999). This study followed individuals born from 1954 to 1965 over the period from 1970 to 1991 for schizophrenia. In this figure, we see a cohort effect in the general decline in incidence over birth years – with each age group trending downwards – and the age effect with ages 16–17 years at lowest risk, and ages 20–21 and 22–23 at higher risk.

in later historical periods. The shift from younger age at maximum risk to older age at maximum risk over historical periods may have led some to conclude that, while tuberculosis was on the wane, it had become more lethal to the elderly. Analysing trends by generation, however, revealed that in each generation the peak in rates occurred between 20 and 30 years of age, and that over each succeeding generation rates were declining in an orderly fashion. The disease had not undergone a metamorphosis, nor had the elderly developed a peculiar susceptibility to the disease; instead, experience had changed over successive generations. Understanding this also pointed to early life experience as crucial to risk for the disease.

Graphical display analysis is useful in visually discriminating period and age, or chort and age effects. Data displayed as in Fig. 1.1 discriminates period and age effects, and data displayed as in Fig. 1.2 discriminates cohort and age effects. However, there are limitations to assessing these three effects simultaneously.

Period, age and cohort effects may all be influential in a given secular trend, as is made obvious in the example of tuberculosis. Using ordinary graphical displays, it is not possible to control two while examining the third. Thus, in Figure 1.1, while examining period trends we control for age but not for cohort effects; and in Figure 1.2, while examining cohort trends we control for age but not for period effects. Statistical methods have been developed to examine the three effects simultaneously (e.g. Holford, 1983; Clayton and Schifflers, 1987). However, these methods

require additional complex assumptions. Notwithstanding its limitations, graphical display still provides a direct and understandable method of analysis (Case, 1956).

Life-course effects

The structure of age–period–cohort trends emerges from the multitudes of individual life-course effects. Life-course effects capture the longitudinal component of human biological as well as social exposures and existence to the point of disease or risk assessment. Individual life-course effects are framed at each given age within a unique historical period, creating an experience set that is particular to each generation.

Evidence and reason suggest that socioenvironmental factors influence health risk over the lifespan, contributing as early as the prenatal period to adult disease (Kuh and Ben-Shlomo, 1997; Marmot and Wadsworth, 1997; Davey Smith et al., 1997). Evidence for prenatal and childhood exposures contributing to risk of adult disease is perhaps more well known in psychiatry than other fields of study. For example, prenatal nutritional and viral exposures have been linked to risk of schizophrenia, and childhood neglect, abuse and loss have been linked to risk of adult depression. The notion that many prenatal and childhood exposures are socially patterned is also widely accepted. From this starting point, the individual progresses through time, accumulating risk associated with age and historical period.

The relative importance of prenatal, childhood and adult experience in shaping risk for disease, and the importance of cumulative experiences, may vary with specific diseases. Studies at the individual level, for example, indicate that childhood social status and related childhood pulmonary exposures are relatively more influential in tuberculosis, whereas adult social status and adult behaviour are more influential in lung cancer (Davey Smith, 2001). In the case of cardiovascular mortality, there is evidence for independent risk attached to socioeconomic adversity during different phases of life, and for the accumulation of risk associated with socioeconomic adversity (Davey Smith et al., 1997). For this reason, a longitudinal view of individual development is necessary to identify critical periods, to develop a schema for understanding the accumulation of risk and to translate 'vulnerability' to disease into a more specific set of risk factors. This was described by G. Davey Smith in 2001:

> Human bodies in different social locations become crystallized reflections of the social experiences within which they have developed. The socially patterned nutritional, health and environmental experiences of the parents and of the individuals concerned influence birthweight, height, weight and lung function, for example, which are in turn important indicators of future health prospects. These biological aspects of bodies (and the history of bodies) should be viewed as frozen social relations . . .

REFERENCES

Case RA (1956) Cohort analysis of mortality rate as an historical or narrative technique. British Journal of Preventative Social Medicine 10, 159–171.

Castle DJ, Scott K, Wessely S, Murray RM (1993) Does social deprivation during gestation and early life predispose to later schizophrenia? Social Psychiatry and Psychiatric Epidemiology 28, 1–4.

Clayton D, Schifflers E (1987) Models for temporal variations in cancer rates, II: age–period–cohort models. Statistics in Medicine 6, 469–481.

Davey Smith G (2001) The uses of 'Uses of Epidemiology'. International Journal of Epidemiology 30, 1146–1155.

Davey Smith G, Hart C, Blane D, Gillis C, Hawthorne V (1997) Lifetime socioeconomic position and mortality: prospective observational study. British Medical Journal 314, 547–552.

Dohrenwend BP, Levav I, Shrout PE et al. (1992) Socioeconomic status and psychiatric disorders: the causation–selection issue. Science 255, 946–952.

Done DJ, Crow TJ, Johnstone EC, Sacker A (1994) Childhood antecedents of schizophrenia and affective illness: social adjustment at ages 7 and 11. British Medical Journal 309, 699–703.

Goldberg EM, Morrison SL (1963) Schizophrenia and social class. British Journal of Psychiatry 109, 785–802.

Holford TR (1983) The estimation of age, period and cohort effects for vital rates. Biometrics 39, 311–324.

Hollingshead AB, Redlich FC (1958) Social Class and Mental Illness. New York: Wiley.

Jones P, Rodgers B, Murray R, Marmot M (1994) Child developmental risk factors for adult schizophrenia in the British 1946 birth cohort. Lancet 344, 1398–1402.

Kuh E, Ben-Shlomo Y (1997) A Life Course Approach to Chronic Disease Epidemiology. Oxford: Oxford University Press.

Lapouse R, Monk MA, Terris M (1956) The drift hypothesis and socioeconomic differentials in schizophrenia. Mental Diseases 46, 978–986.

Link BG, Dohrenwend BP, Skodol AE (1986) Socio-economic status and schizophrenia: noisome occupational characteristics as a risk factor. American Sociological Review 22, 288–292.

Makikyro T, Isohanni M, Moring J et al. (1997) Is a child's risk of early onset schizophrenia increased in the highest social classes? Schizophrenia Research 23, 245–252.

Marmot MG, Wadsworth MEJ (eds.) (1997) Foetal and early childhood environment: long-term health implications. British Medical Bulletin 53, 1–227.

Rose G (1992) The Strategy of Preventive Medicine. Oxford: Oxford University Press.

Schwartz S (1994) The fallacy of the ecologic fallacy: the potential misuse of a concept and the consequences. American Journal of Public Health 84, 819–824.

Schwartz S, Carpenter KM (1999) The right answer for the wrong question: consequences of type III error for public health research. American Journal of Public Health, 89, 1175–1180.

Schwartz S, Susser E (2001) What is a cause? In Psychiatric Epidemiology: Concepts and Method, Susser E, Bromet E, Morabia A, Schwarz S, Gorman J (eds.).

Susser M (1973) Causal Thinking in the Health Sciences. London: Oxford Medical Publications.

Suvisaari JM, Haukka JK, Tanskanen AJ, Lonnqvist JK (1999) Decline in the incidence of schizophrenia in Finnish cohorts born from 1954 to 1965. Archives of General Psychiatry 56, 733–740.

Timms D (1998) Gender, social mobility and psychiatric diagnoses. Social Science and Medicine 46, 1235–1247.

Turner RJ, Wagenfeld MO (1967) Occupational mobility and schizophrenia: an assessment of the social causation and social selection hypotheses. American Sociological Review 32, 104–113.

van Os J, Driessen G, Gunther N, Delespaul P (2000) Neighbourhood variation in incidence of schizophrenia. Evidence for person–environment interaction. British Journal of Psychiatry 176, 243–248.

Wiersma D, Giel R, deJong A, Slooff CJ (1983) Social class and schizophrenia in a Dutch cohort. Psychological Medicine 13, 141–150.