

Invited editorial

Psychiatric epidemiology: a Scandinavian contribution to international psychiatry

Introduction

First, a word about Scandinavia.

Scandinavia comprises three countries: Denmark, Norway and Sweden. Together with Finland and Iceland, they constitute the Nordic countries, that is Finland and Iceland are not part of Scandinavia.

For over three quarters of a century, psychiatric epidemiology has been a Scandinavian parade discipline, and this is what has been chosen as the topic for this editorial. By making this selective and therefore exclusive thematic choice, major Scandinavian contributions will not be mentioned; the choice leaves us no possibility for discussing for instance lithium treatment research under the lifelong enthusiastic leadership of late Danish Mogens Schou. Nor will we find opportunity to include the work on monoamines by our pride, Swedish Nobel laureate, Arvid Carlsson.

As Scandinavia does not include Finland and Iceland, nor will we find possibilities for highlighting, for example, the influential Icelandic and Finnish birth-cohort studies.

Diagnostic culture

Scandinavian psychiatry has akin to international psychiatry in general a German-Swiss background, however, since the 1980s being gradually replaced by an operationalizing diagnostic culture. After less than two decades of official use of the ICD-10 (ICD = International Classification of Diseases), it is this author's impression that a (dis)belief in Scandinavian psychiatry that the ICD-10 (and DSM-IV) statistical concepts called diagnoses exist *per se*, gradually disseminates. When we introduced the ICD-10 in Denmark on January 1, 1994, this was definitely not the idea; the central idea was to offer clinicians and researchers a tool giving them the possibility to talk about the same 'thing' when using classificatory language. Psychiatrist

Aksel Bertelsen, director of the WHO Centre for Psychiatric Education and Research in Aarhus, Denmark through many years, and the present author were responsible for the introduction of the ICD-10 in Denmark, and our intention was to bring an end to the idiosyncratic state of affairs in which 'every psychiatrist has their own private diagnostic definitions' and by using operationalized diagnoses we would enable researchers to better communicate in their search for biological, psychological and social causes for psychiatric diseases.

A major benefit of the ICD-10 in Scandinavia has been a thorough and systematic psychopathological training. Another major advantage of this systematic as opposed to individual and idiosyncratic way of thinking about psychiatry has encouraged the growing acceptance of the mentally disordered person as biological beings. It has also spawned the growth of neuropsychiatric science, which in many places in Scandinavia was non-existent and possibly 'forbidden' in an era of psychodynamics and social psychiatry that dominated until as late as mid-1990.

Reactive psychosis

One of the things we lost by introducing operationalized diagnoses was the reactive psychosis – or the psychogenic psychosis, a concept based on Jasper's triad: a catathymic trauma – a psychogenic (psychotic) reaction – and normalization when the trauma disappears (or is dealt with). The concept of reactive psychosis, based on works by Danish Wimmer early in the 20th century and Færgeman from post-World War II, is described in 1968 by Ødegaard (1), and again in 1974 by Danish Erik Strømgren (2), who incidentally was one of the founders of modern psychiatric epidemiology. It was later thoroughly validated by Norwegian

psychiatrist Dahl (3) in 1994 and was widely used in the 1960s, 1970s and 1980s. From the Danish Psychiatric Central Research Register, implemented in its modern electronic person-identifiable version in 1969 by Dupont and Strömngren and further modernized over the period 1987–2004 by the present author (4, 5) in collaboration with the Danish National Board of Health, we know that e.g. reactive psychoses constituted 2.9% of 4996 diagnoses among men and 4.8% of 5862 among women hospitalized on a census day in 1982 (6).

Early migration studies

Above we mentioned the Norwegian Ødegaard, a performer of classical Scandinavian epidemiology who in particular is known for his pioneering work within transcultural psychiatry (7). Ødegaard found an increased risk of psychosis among Norwegian immigrants to the United States. He hypothesized that psychological environmental factors played an etiological role. In 1932, this thinking was relatively new, sprouting from psychodynamic thinking, and by accepting the epidemiologically based findings, his research aimed at what later became *the* paradigm of causative theories for psychosis as hypothesized by Zubin in the diathesis stress model. The design for Ødegaard's study (7) has subsequently been developed and sophisticated by Murray's group in their studies of Caribbean second-generation migrants to London.

Genetic epidemiology

Scandinavian psychiatrists have made a substantial contribution to psychiatric genetic epidemiology.

Together with US colleague Seymour Kety, Copenhagen psychiatrist Fini Schulsinger investigated the influence of environmental and hereditary risk factors for schizophrenia with the aide of a cohort of adoptees (8), while Oslo psychiatrist Ejnar Kringlen tested the same hypothesis in twins (9).

From Denmark, aforementioned psychiatrist Aksel Bertelsen has with different research groups and together with US colleagues made notable contributions to psychiatric genetic epidemiology using twin study methods (10) and dual mating methodology (11). In a highly cited study (10), Aksel Bertelsen and his colleagues used data from a combination of the Danish Twin Register with the Danish Psychiatric Register in their early

manual versions. He identified individuals given a psychiatric diagnosis and examined all available case material and interviewed the probands. Aksel Bertelsen and his coworkers calculated the concordance rates in a number of ways and found, for example, a pair-wise calculated difference of concordance for manic depressive disorders between DZ twins, 0.17, and MZ twins, 0.58. The study, published in 1977, can still 30 years later serve as a model for genetic epidemiological research with its combination of register data and data from clinical examination drawing on all available material. Furthermore, the then publishing editor of the *British Journal of Psychiatry* did not suffer from the currently widespread ailment known as 'editor's syndrome' that manifests as a reflex response when an editor is presented with a manuscript: 'The manuscript must be substantially shortened'. The article gives all the necessary information, it uses time and space for the thorough description of material and methods, and a discussion worth reading not mentioning the very detailed data documentation. May we recommend this article among the material for different training courses – including courses for editors.

Besides Bertelsen's studies, the results from Schulsinger and Mednick and their group's high-risk study have had a remarkable impact on ethological research in schizophrenia. They followed a cohort of 207 sons and daughters of mothers with schizophrenia and 104 controls from teenage years till their early forties, finding 21% and 3% respectively in the two groups developing schizophrenia spectrum psychotic disorders rising to 43% and 8% when including schizophrenia spectrum personality disorders (12).

Register research

The success of Scandinavian epidemiological research including psychiatric epidemiology, especially during the past two or three decades, is based largely on longitudinal and person-identifiable databases.

In the early 1990s, computer technology became so advanced that personal computers with a sufficient capacity and speed became available, making it possible at a low cost to use the enormous amount of data stored in the numerous person-identifiable registers in Scandinavia. Danish Preben Bo Mortensen and his Aarhus group have taken modern register linking methodology to its brink. An example of this is a study in which he identified risk factors for suicide by linking a labor

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market register containing longitudinal data about income, unemployment, education and cohabitation with the Danish Psychiatric Central Research Register and the Danish Register for Causes of Death. One key finding was that the strongest predictor of all for suicide was 'having been discharged within 8 days before suicide from a psychiatric hospitalization'. This had an incidence rate ratio of 337 when correcting for all variables included in the study. The other very interesting finding was that there were only minor differences between the risk for suicide among the different psychiatric diagnoses (13).

Another excellent example of linkage studies is Ösby's (14) study on time trends in mortality in schizophrenia. Ösby and his Stockholm group used the same technique linking the in-patient register for Stockholm County with Swedish Death Register. He showed an increase in standard mortality rate over time for all causes of death in patients with schizophrenia and underlined, based on the finding of increased death from cardiovascular disease that the somatic health of these patients was deteriorating.

Californian psychologist Sarnoff Mednick designed a study in which the Danish registers could be used to test the influenza-schizophrenia hypothesis. The authors performed an ecological epidemiological study combining the weekly national statistics about reported – aggregated – data on influenza cases in the country since 1910 and the person-identifiable data about schizophrenia cases in the psychiatric register. The analysis showed a correlation between mothers having been pregnant during rises in national influenza occurrence and increased rate of schizophrenia incidence among the offspring years later, suggesting a correlation between influenza exposure during fetal state and the later development of schizophrenia (15).

Clinical register-supported studies

If register linking research including several registers with huge numbers of data in each represents the highest level of methodological sophistication. The highest level of scientific sophistication in Scandinavian epidemiological research is reached by the technique in which huge clinical cohorts are followed (also) by help of registers. In this type of research, the problem as regards low validity of data in registers (especially diagnoses) is partly overcome by the clinically collected research data when examining the probands, especially at index, and the problem of loss to follow-up invalidating

clinical studies is overcome by using (also) registers. This type of research is superbly represented by Göteborg psychiatrist Peter Allebeck and his group. Approximately 50 000 men conscripted in 1969/1970 for service in the Swedish army were followed up for 26 years by help of registers. Register outcome data were correlated to the systematically collected basic data from examinations and tests at conscription, and a dose-dependent linear association between cannabis use and the subsequent development of schizophrenia was documented (16, 17).

Strengths and limitations of register research

The Scandinavian registers covering almost all aspects of life are a goldmine for hypothesis-founded register linkage studies – and a horror scenario for unqualified 'fishing trips'.

Large-scale person-identifiable register linking, which has been the Scandinavian epidemiology flagship for now two decades has more advantages: large samples, longitudinal perspective, low loss to follow-up and possibilities for extensive confounder control.

However, the limitations – described at an early stage in the development of the register linkage research era by Munk-Jørgensen and Mortensen (18) in 1992 are now becoming more obvious: compromised data validity because data are collected for administrative, nonscientific research purposes, for example, the diagnoses of schizophrenia and bipolar disorder (until 1994 manic depression) are hardly the same in 2007 as they were in 1970, the first full year of registration to the electronic version of the Danish Psychiatric Central Research Register.

Health care and disease registers are defined by services not by occurrence of diseases in the population, for example, of the depressed individuals in a community, only approximately 5% – the most severe cases – get into contact with the hospital-based system and therefore are registered, that is, it is very difficult, not to say impossible, to do register research about depression.

In a recent review of the literature about validation of existing register research, only 14 international studies were found of sufficient quality as to data validation (19). With a certain pride, we notice that five Scandinavian studies were among the 14 (19). This discouraging finding that extremely few studies performed a sufficient data validation was commented by Parker as an '... ongoing need to examine rather than assuming the validity of any particular database' (20).

Scandinavian tradition for longitudinal research

Finally, we would like to bring two examples on how continuity and long-term perspective is an integrated part of Scandinavian psychiatric epidemiological research, both of them from Sweden.

The first example is from Göteborg. Gunnar Skoog examined a group of patients with obsessive-compulsive disorder in the late 1940s and early 1950s; later on in the early 1990s, the cohort was followed up by Gunnar Skoog and his son Ingmar Skoog and published in a 40-year follow-up (21). Among their results, it is worth mentioning the optimistic finding that 20% recovered completely and 28% recovered with subclinical symptoms – in an era with limited treatment possibilities.

In 1947 psychiatrist Essen Möller together with, among others, Olle Hagnel examined 2550 inhabitants in a parish outside Lund in Southern Sweden (22, 23). The study, given the name *The Lundby Study* is the sole among the longitudinal personal follow-up population studies founded in the immediate postwar period in the 1940s and 1950s that is still currently active. Recently, a 50-year follow-up including personal interviews, use of case material and register data has been performed (24), and a series of interesting publications are on their way.

Future psychiatric epidemiology in Scandinavia

It is very difficult to guess, especially about the future, and guessing about the future quite often is an extrapolation of trends that we already know about. However, this author sees some advantages in keeping the widespread high level of epidemiological thinking as an integrated part of clinical psychiatry and psychiatric research in the future underlining epidemiology as a methodology, to a lesser degree using the concept as we did in the past: as descriptive epidemiology. We have the possibilities in Scandinavia for collecting very large cohorts counted in ten and hundred thousands of individuals thoroughly studied by research interviews and examinations. These data collected in large research databases together with biomaterial in biobanks will be of great importance. It should be an advantage that cohorts were collected on multicentre basis instead of spreading the energy in creating several smaller databases. Our extensive and intensive registration of our populations offers the possibilities for identifying individuals repeatedly over time giving us the possibilities for clinical follow-ups characterized by very low loss to follow-up.

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