International Trends of Psychiatric Epidemiology

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Abstract: Psychiatric epidemiology traditionally seems to be insufficient to definite measurement and case definition. Since 1900s, there had been numerable studies on prevalence and incidence of mental disorders according to diagnostic measurements. However, there is no consistent and clear consensus on psychiatric epidemiologic findings. In spite of difficulties in measurement issues, psychiatric epidemiology has advanced from vague case definition by expert’s bias to relatively concise method using scientific technology. Especially, biological advancement and genetic epidemiology made psychiatric epidemiology clearer than past several decades. Even though the more complicated methods on psychiatric epidemiology have good merits to measure between psychopathology and diagnosis, there are many limitations to explain the relationship between social, environmental factors and biological vulnerabilities. In the future direction of psychiatric epidemiology, collaborating measurements biological markers with psychosocial factors will make explain the etiological background of mental disorder easier than past years.

Key words: Psychiatry, Epidemiology, Trends, Review, and Mental disorders

Psychiatr Invest 2005; 2 (1): 14-21

Introduction

Epidemiology is concerned with understanding and controlling disease epidemics by investigating empirica-
population. Despite the serious methodological problems of identifying and classifying disorders independently of treatment status, these first and second-generation studies made important contributions. Most of these studies concentrated on current prevalence and found that prevalence rates of various types of psychiatric disorders varied consistently by genders, socioeconomic status, and location.

Starting around 1980, a third generation of studies began. As with the first and second generation of studies coincided with still another set of dramatic changes in nomenclature. These changes were summarized in the DSM-III-R, DSM-IV and ICD-10.

In spite of advancing methodology in descriptive and analytic or experimental epidemiology, there have been another great changes in entire psychiatric epidemiology since 1990. Robin suggested that the greatest hope for breakthrough in our understanding of the etiology of mental disorders would come from genetic epidemiology. Linkage studies have been unable to identify a single specific gene or gene marker for any major mental disorder after more than ten years of active research. However once such markers are identified, integration of psychiatric epidemiology with population genetics will be valuable in a number of ways, but it is not clear when this will occur. In this paper, the authors will suggest that how brief explanation of psychiatric epidemiological history and important methodology have been changed and where the future direction of psychiatric epidemiology will go.

Historical remarks of psychiatric epidemiology

In 1978, Michael Shepard gave a lecture in which it was necessary for him to argue from first principle for the need for epidemiological research within clinical psychiatry. He listed the contributions of psychiatric epidemiology as follows: 1) the completion of the spectrum of disease, 2) the establishment of outcome, 3) the actual assessment of morbidity risk, 4) the evaluation of efficacy of treatment, and 5) the conceptual construction of diagnosis and classification. The first two aims refer to descriptive research that counter the bias in clinical samples-enumerating disease frequency and describing the range of symptomatology and the natural history of psychiatric disorders as found in the general population. The third aim is to discover who is at risk and by how much the chance of disease increases due to any particular risk factor, either for an individual or for a population. The fourth aim is to prove which interventions might be helpful-using strategies to eliminate the investigator’s own prejudice and the biases involved in recruiting selected subjects for study. The last aim comes from the epidemiologist’s frequent failure in the field to identify clear-cut disorders, when applying diagnostic descriptions derived from hospital populations.

On the other hand, Wittchen described the major progresses of psychiatric epidemiology in the 1990s as follows: 1) availability of large general population studies, 2) increasingly sophisticated sampling, design and statistical procedures, 3) international collaboration, 4) crude documentation of impairments and disabilities, 5) crude documentation of poor recognition and interventions, 6) improvements in diagnostic instruments and contributions to psychology and diagnostic classification, 7) slowly increasing number of prospective-longitudinal and family genetic studies, and 8) contributions to nosological research.

In broader concept, epidemiological studies must be linked and influenced by social and health policy within its society. Health policy at national level will identify the range of health, morbidity, disability and mortality issues, the overall framework for implementing the policy in the relevant settings. Thus, mental health policy is increasingly recognized as meriting a long overdue attention in many countries, partly because of the realization of the economic and social burden of mental disorder for countries.

Jenkins tried to find information need for mental health policy from both relatively wealthy and low-income countries using 6 indices: the social and physical context, epidemiology and disability, needs for care, service inputs, service processes and healthy outcomes. In this article, epidemiological findings showed that mental health and mental disorders were related to the environment both in its structural physical sense and in the sense of the social processes connected to and influenced by particular settings. Also this article emphasized that the importance of mental health policy addressing the key role of primary care, the social context and social consequences of disorder, the importance of addressing ser-
vices for children, the need to reduce premature mortality from suicide and physical illness. Thus epidemiology can contribute to general policies on employment and unemployment, housing and homelessness, education and woman’s issues.13

As the traditional view was the genes and environment act upon disease independently, research has been focused on how much each contributes. However, a new possibility is that genotype acts to produce a disease, but also influences the environment in which the individual exists. The second possibility is that the genotype acts as a modifier upon the way exposure influences disease onset. Evidence is now accumulating to suggest heritability of what was thought to be a random exposure, the type and frequency of life events. McGuffin14 first reported that the experience of depressive symptoms and the tendency to experience adverse life were due to familial history of mental disorders. Secondly, it is possible that genes can determine how we cope, solve problems and seek support, actions that modify the impact of an adverse event upon the chance of disease. For example, coping mechanisms have been estimated by Kendler15 to have a heritability of approximately 30%.

Quantitative genetic studies indicate that genetic influences are important for both psychiatric disorders and behavioral traits. Specific gene loci can be tested for associations with both psychiatric risk and behavioral traits by means of molecular genetic techniques. Therefore, advances in quantitative and molecular genetics now permit more careful examination of genotype-environment interaction and correlation. However, studies combining molecular genetic strategies with measurement of the environment are still at an early stage, and results must be awaited16.

Nowadays, there is also another area in psychiatric epidemiology. Pharmacoepidemiological studies investigate the effects of pharmacological agents in human populations, applying the same designs: case-control, prospective cohort and measures of association as other epidemiological studies. They can help to determine the effectiveness of drugs in clinical settings. Unlike clinical trials, which include only patients who are willing to participate in a controlled investigation, pharmacological databases contain records of all patients treated in a particular clinical setting.27

**Trends of case identification and classification**

Psychiatric epidemiology, like other epidemiological study, is dependent on the accuracy of diagnosis. In the absence of consensus about how to identify and classify psychiatric disorders, first and second generation studies tended to pioneer its own unique methods and procedures for identifying cases, with very little attention to problems of validity6, 7. In the best known of the second generation studies,18, 19, US investigators tended to bypass the problems involved in identifying and classifying different types of psychiatric disorders on the basis of vague descriptions and inadequately detailed systems of nomenclature. However, Wing et al20 developed the accurate operational criteria for specific diagnostic types on the basis of existing nomenclature: Present State Examination (PSE). Semi structured diagnostic interview and rating procedures such as those of the PSE and Schedule for Affective Disorders and Schizophrenia (SADS)21, developed for clinical research with patients and designed to be used by experienced clinicians, found their way into several epidemiologic studies.22

Such efforts which were contributed to develop the accurate and operational diagnostic case definitions since 1970s were as follows: General Health Questionnaire23, Hopkins Symptom Checklist24, Center for Epidemiologic Studies Depression Scale25, and Psychiatric Epidemiology Research Interview26. On the base of these developments, there has been a great advancement for assessing psychiatric disorders and identifying caseloads since 1980s. One is Diagnostic Interview Schedule (DIS)27, and the other is Composite International Diagnostic Interview (CIDI)28: so called to third generation studies of psychiatric epidemiology.

In the absence of laboratory tests for identifying and classifying psychiatric disorders, all of these approaches are based on personal interviews. There is controversy about their relative merits and about trade-offs made in the interest of economy, such as use of data derived from lay interviewer methods versus clinician interviewer methods for arriving at diagnoses29.

Case identification and classification measures actually used even now in third generation studies are often compromises between what is practical and what is optimum for diagnoses based on evidence of symptoms elicited by interview. However, it is clear that there is an array of
alternative and combination approaches that represent advances in case identification and classification that was simply not available to investigators during the conduct of first and second-generation research in psychiatric epidemiology.

This focus on the accurate assessment of signs and symptoms will put a greater premium on the use of skilled interviewers and clinically experienced observers. Establishing accurate measures of signs and symptoms will ensure that measures will not be out of date with changes in rationales for how they should be combined to indicate particular diagnoses.

While studying the case identification and classification, there is another important issue, which occupied major problems in statistical power: sampling design. Since 1980s, DIS and CIDI had contributed the accurate case identification. However, there is a limitation to interpret the results from field epidemiological study. Even the largest of epidemiological samples is not adequate for the intensive investigation of important but relatively rare disorders such as schizophrenia. Problems of selection bias can be severe in DIS and CIDI studies.

The only way to assess such biases is through comparison of larger patient samples with smaller but more representative samples of persons diagnosed with the same disorder in epidemiologic studies of birth cohorts drawn from general population. In the future, there will be increased such design to reduce the selection biases under great efforts to case identification. Table 1 shows the historical changes of psychiatric epidemiology according to diagnostic or case definition and identification.

### Trend of methods in psychiatric epidemiology

Epidemiological methods are particularly helpful in confusing cause-effect association between mental disorders and biological, environmental, and psychosocial risk factors. These methods are also ideal for studying the natural course and the treatment outcome of mental disorders. In this regard, the course of illness helps with psychiatric nosology by differentiating psychiatric conditions in terms of response to treatment and outcome.

The major issue in investigating psychiatric epidemiology is the measurement problem. As described above phrases, many epidemiologists have tried to improve the diagnostic criteria for accurate and interactive communicable case definition. One goal of epidemiological studies is to estimate the degree of association between two variables or between risks and outcomes. The most commonly utilized measure of association is relative risk,

<table>
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<tr>
<th>Instrument or hallmark studies</th>
<th>Descriptions</th>
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<tr>
<td><strong>First (Before World War II)</strong></td>
<td>Stress on genetic and ethnic factors</td>
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<tr>
<td>Jarvis E (1855)²</td>
<td>Stress on environmental factors</td>
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<td>Elder GH (1974)²</td>
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<tr>
<td><strong>Second (1945-1970)</strong></td>
<td>Focus on identifying and classifying disorders</td>
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<td>Srole L et al (1962)³</td>
<td>: vague and inadequate descriptions</td>
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<td>Leighton DC (1963)⁴</td>
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<td><strong>Third (1970-1990)</strong></td>
<td>First semi-structured diagnostic system</td>
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<tr>
<td>Wing JK et al (1974)⁵</td>
<td>Large-scale investigation</td>
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<td>Wittchen H-U (1994)⁷</td>
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<td><strong>Fourth (1990-present)</strong></td>
<td>Strong emphasis on the search for specific risk factors, both biological and psychosocial</td>
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<td>Clinical Epidemiology</td>
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<td>Genetic Epidemiology</td>
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* This format is based on Dohrenwend’s description and summarized by the authors.

¹Insanity and idiocy in Massachusetts: report of the Commission on Lunacy
²Children of the Great Depression
³Mental Health in the metropolis: Midtown Manhattan Study
⁴The Character of danger: psychiatric symptoms in selected communities
⁵Present State Examination and Catego Program (PSE)
⁶National Institute of Mental Health: Diagnostic Interview Schedule (DIS)
⁷World Health Organization: Composite International Diagnostic Interview (CIDI)
which is the most important statistical power in psychiatric epidemiology. In field trials, there are many structural and sampling biases that are difficult to practice in reality. The basic epidemiological methods to refine case identification are reasonable measures of frequency including prevalence and incidence.

In recent days, a new trend has been appeared like special applications of epidemiologic method: clinical epidemiology\textsuperscript{30}. Although different definitions of clinical epidemiology exist, the one is the application of epidemiological principles and methods to problems encountered in clinical medicine. Such as odds ratio, relative risk, positive and negative predictive value as well as epidemiologic databases are adapted to assist bedside clinical investigation and decision making with regard to the individual patient or clinical groups\textsuperscript{2}.

In spite of the advancement of scientific methodology, there has been a strong evidence and consistent epidemiologic finding between socioeconomic inequalities and mental disorders. One of the most consistent findings in psychiatric epidemiology prior to 1980 has been that socioeconomic status (SES) was inversely related to the recent prevalence of a variety of important types of disorder. The findings raised major issues about the role of adversity in these disorders. In recent years, however, research interest in these issues has been declining. At the same time, marked changes have been taking place in the case identification and diagnostic procedures available for epidemiological research. These changes in diagnostic concepts and methods have led to a change in the facts that gave rise to the issues about the role of SES\textsuperscript{34}.

For example, socioeconomic inequality in depression is heterogeneous and varies according to the way psychiatric disorder is measured, to the definition and measurement of SES, and to contextual features such as region and time. Nonetheless, the authors found compelling evidence for socioeconomic inequality in depression\textsuperscript{31}.

There is also the SES and schizophrenia. For example, singleness and unemployment increase the risk of schizophrenia. Schizophrenia subsequently increases the risk of singleness and unemployment. Finally, schizophrenia hinders social achievement long before the first admission. The first hospital episode is followed by a period during which social status does not deteriorate further except for the transition into disability pension\textsuperscript{32}.

In the future study of socioeconomic status and mental disorders, multidimensional approach linking psychosocial aspects and biological markers will make the epidemiological findings clearer than past years.

**Advancement of Genetic epidemiology**

It has emerged as great advance discipline since 1970s and is currently viewed as the study of the role of genetic factors and their interaction with environmental factors in the occurrence of disease in human population.

It uses two main types of research strategy. One is population-based such as association studies comparing marker gene distributions in samples of unrelated affected individuals and samples of unrelated controls like classical case-control studies. The other is family-based such as transmission of a disease phenotype or trait in a pedigree is examined for a linked transmission of a genetic marker\textsuperscript{33}. With major advances in the complete sequencing of the human genome and recent innovations in molecular research technology, the prospect of detecting and cloning within next decade, genetic epidemiology will serve the etiology of mental disorders. Especially we refer to molecular epidemiology as the utilization of genetic markers in large, population-based studies with the aim of investigating associations between DNA polymorphisms and behavioral phenotypes defined by psychiatric diagnosis or quantitative traits. Throughout Human Genome Project, we also call to its area as human genome epidemiology\textsuperscript{2}.

Interesting findings about genetic epidemiology are follows: locating disease-related genes, allelic association studies for complex traits and measuring the phenotype. More often and especially in psychiatric disorders, there is insufficient prior knowledge of candidate genes. The search for their chromosomal location is then based on linkage analysis or methods for the detection of allelic association. Linkage analyses are most powerful when applied to single gene disorders but are sensitive to inaccurate definition of the phenotype and to incorrect assumptions about the penetration and mode of inheritance of the disease. Allelic association studies complement linkage and are another important method to locate genes. A well-known example of allelic association is the increased frequency of specific HLA antigens in several diseases. Detecting association is therefore a powerful for mapping disease genes over short genetic dis-
tance. Association studies also have power to detect genes of small effect that contribute only a small proportion to the relative risk of a disorder. Epidemiologists have known that the biological domain might be important in etiology, but for the common mental disorders it has been largely passed over. Properties of the adult brain, whether innate or molded by environmental exposures, have only rarely been accessible. With the advances in molecular genetics, this is changing. For epidemiology, there is now the possibility of bringing molecular genetics into studies of etiology. Because of the significance of this development, we present a critical assessment of the prospects for population-based research using molecular genetics, the work already reaching publication and the methodological issues that are arising.

**Trends of Linkage study between descriptive and genetic epidemiology**

Several important results have consistently emerged from third generation epidemiological studies such as NIMH’s DIS and WHO’s CIDI surveys. The first is that mental disorders are among the most prevalent classes of chronic diseases in the general population. The second is that mental disorders typically have much earlier ages of onset than other chronic diseases. The third is that there is an important correlation between environmental and genetic factors.

Since the mid 1970s epidemiological period, the strongest evidence acquired from three behavioral genetics (family, twin, and adoption studies) has focused on many psychiatric disorders. However, there is also another evidence that genetic factors alone cannot account for development of psychiatric disorders.

Psychiatric epidemiology is a key mental health discipline that has adopted and developed a variety of methods and procedures for the study of complex mental disorders in conceptual and methodological advances of molecular biology and neuroscience within the population-based and social framework of epidemiology as a basic science of public health.

The next decade will witness shifts in approaches of both epidemiology and genetics to address sources of complexity of the mental disorders. Descriptive genetic epidemiology will evolve into analytic genetic epidemiology by shifting the key questions from estimation of the magnitude of mental disorders to identification of risk and protective environmental factors that may be informative for both etiology and prevention. Genetics research will expand to population-based studies for complex disorders and will employ designs and methods that incorporate sources of complexity.

**Role of culture on psychiatric epidemiology**

The debate on the role of culture on psychiatric epidemiology has evolved considerably in the past two decades. There is now a general consensus that the integration of the universalism and culturally relativism approaches, and their methodologies, is required to generate a truly international psychiatric epidemiology.

The large body of research investigating the influence of culture on the epidemiology of depression has produced a number of key findings: the clinical presentation of depression in all cultures is associated with multiple somatic symptoms of chronic duration; psychological symptoms, however, are important for diagnosis and can be easily elicited. The diagnostic differentiation between depression and anxiety in general health care settings is not clinically valid. Culturally appropriate terminology for depression can be identified and their use may improve levels of recognition and treatment compliance. It is also evident that culture is only one factor in the difference between, and within, human societies, which have a bearing on the epidemiology of depression. Other factors, which may interact with culture, such as gender and income inequality, are major risk factors for depression. Future international research must focus on two themes: 1) intervention studies including cost-effectiveness outcomes; and 2) research aiming to bridge the gap between regional public health priorities and the concern that psychiatrists have about depression.

**Future direction and conclusion**

Major advances in descriptive psychiatric epidemiology in recent years include the development of reliable and valid fully structured diagnostic interviews, the implementation of parallel cross-national surveys of the prevalence and correlates of mental disorders, and the initiation of research in clinical epidemiology.

Remaining challenges include the refinement of diag-
nostic categories and criteria, recognition and evaluation of systematic underreporting bias in surveys of mental disorders, creation and use of accurate assessment tools for studying disorders of children, adolescents, the elderly, and people in less developed countries, and setting up systems to carry out small area estimations for needs assessment and program planning.

Advances in analytical and experimental epidemiology have been more modest. A major challenge is for psychiatric epidemiologists to increase the relevance of their analytical research to their colleagues in preventative psychiatry as well as to social policy analysts. Another challenge is to develop interventions aimed at increasing the proportion of people with mental disorders who receive treatment. Despite encouraging advances, much work still needs to be conducted before psychiatric epidemiology can realize its potential to improve the mental health of populations1, 30.

The current, ‘fourth generation’ of psychiatric epidemiological research is characterized by a strong emphasis on the search for specific risk factors, both biological and psychosocial. Just around the corner, there is an emerging ‘fifth generation’ of studies, which are aiming to integrate recent advances in understanding the human genome into the search for causes of psychiatric disorders on a population basis; i.e. molecular epidemiology or human genome epidemiology.

Current psychiatric epidemiological research is increasingly orientated towards so-called ‘strategic populations’ that may be more informative with regard to teasing out causative pathways in psychiatric illness such as genetic isolates, samples of specifically configured pedigrees and groups known to be at an increased risk of morbidity. The questions that psychiatric epidemiology aims to answer are not generically different from those that any branch of disease epidemiology attempts to tackle these questions pertaining to the incidence and prevalence of disorders, groups at high or low risk of disease, associations with characteristics of the host and the environment, determinants of disease outcome, and response to specific interventions. Ultimately, establishing the epidemiological ‘signature’ of a disease should provide guidance for laboratory research into its molecular mechanisms. However, psychiatric epidemiology faces challenges that are rarely encountered in other epidemiological investigations. With a few exceptions, the unit of analysis in psychiatric epidemiology, the case is not flagged by a pathognomic or by a disease marker, such as high blood pressure or tumor cytology that could reliably identify case. Instead, the psychiatric epidemiologist has to make sense of subjectively reported symptoms or observed behavior to infer a diagnostic classification of cases. This puts researchers into a sort of ‘double bind’ on one hand, epidemiological leads are important signposts for etiological or pathogenetic research in the laboratory; on the other hand, the value of epidemiological data would be greatly enhanced if valid disease markers for use in the field were generated by laboratory research30. While validated markers to complement the clinical criteria will eventually be forthcoming, a way out of the present difficulty to put all available knowledge about psychiatric disease phenotypes to the best possible use by employing standardized, operational definitions and by constantly updating that knowledge through a close, two-way interaction with clinical and laboratory scientists.

Complementing the human genome project, the human environome project represents the proper agenda for psychiatric epidemiology in the next decade and beyond38.

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