Gender differences in the epidemiology of affective disorders and schizophrenia

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Division of Mental Health and Prevention of Substance Abuse

World Health Organization
Geneva
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NATIONS FOR MENTAL HEALTH:
An Initiative for Mental Health in Underserved Populations

Objectives of Nations for Mental Health

- To enhance the attention of the people and governments of the world to the effects of mental health problems and substance abuse on the social well-being and physical health of the world's underserved populations. A first step is to increase awareness and concern of the importance of mental health through a series of key high profile regional and international events. Secondly, efforts will be devoted to building up the will of the key political authorities to participate. Thirdly, and finally, efforts are to be directed at securing political commitments by decision-makers.

- To establish a number of demonstration projects in each of the six WHO regions of the world. They are meant to illustrate the potential of collaborative efforts at country level, with the view of leading on to projects of a larger scale.

The implementation of the programme depends on voluntary contributions from governements, foundations, individuals and others. It receives financial support from the Eli Lilly and Company Foundation. In addition, financial and technical support is also being provided by the Government of the United Kingdom of Great Britain and Northern Ireland, the Institute of Psychiatry at the Maudsley Hospital of London (United Kingdom), the Free and Hanseatic City of Hamburg (Germany), the Villa Pini Foundation (Chieti, Italy), Columbia University (New York, USA), the Laboratoires Servier (Paris, France) and the International Foundation for Mental Health and Neurosciences (Geneva, Switzerland).

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The World Health Organization's Division of Mental Health and Prevention of Substance Abuse has established an initiative called «Nations for Mental Health» to deal with the increasing burdens of mental health and substance abuse problems worldwide. The main goal of the programme is to improve the mental health and psychosocial well-being of the world's underserved populations (e.g. women, children and adolescents, refugees and indigenous populations and those who suffer from acute or chronic mental illness that is inadequately treated).

During the launching of the world mental health report prepared by the Department of Social Medicine, Harvard Medical School, the United Nations Secretary-General said of the UN Mission: «Our objective is to promote the mental health of and well-being of all inhabitants of the planet». The Nations for Mental Health programme embodies this mission.

Solutions to mental health and substance abuse problems entail a joint mobilization of social, economic and political forces as well as substantial changes in governmental policies related to education, health and economic development in each country. This demands an intense and sustained effort from the nations of the world, through joint cooperation between governments, nongovernmental organizations and the organizations within the United Nations system. The programme is of utmost importance to the work of WHO and is willing to lead and coordinate this ambitious task. Several international meetings and launchings have been organized, in collaboration with other international organizations and academic institutions. A number of demonstration projects related to the programme have already been initiated in several countries. These projects are meant to illustrate and/or demonstrate the potential of collaborative efforts at country level, with the view of leading on to projects of a larger scale.

I am very pleased to present this document as part of the global process of raising awareness and concern for the effects of mental health problems. It is hoped that this important work will be useful in providing health planners and policy-makers with an integrated framework, linked both to specific needs and to epidemiological evidence, for addressing the broad spectrum of issues related to mental disorders and psychosocial problems.

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FOREWORD

by Michele Tansella

For a long time doctors and general practitioners have learned from clinical experience that women receive more services for mental disorder in primary care settings than men do. On the other hand psychiatrists and clinical psychologists are aware that this difference is less marked for specialist mental health services and particularly for hospital-based services. These impressions are confirmed by service research studies: there seems to be good evidence that men come to the attention of health services less often than women, but that men are more likely to be referred for specialist psychiatric care (Goldberg & Huxley, 1992; Jorm, 1995). These service utilization data may have important implications for health policy and service organization. However, they simply indicate the extent of treatment, not the need for treatment (Goldman & Ravid, 1980). The clinicians should therefore go beyond their clinical practice and acknowledge that they need help from epidemiologists and from epidemiologically-based research to be able to understand which sex, or which demographic group within each sex, has the greater risk of experiencing psychological distress and mental illness.

From epidemiological surveys which have attempted to evaluate “true” prevalence by examining random samples of a population and by determining the mental status of the respondents to a questionnaire or interview, these does not appear to be much difference between males and females in the overall prevalence of mental disorders. But evidence does exist that the pattern of the disorders, as well as of psychological symptoms, differs between men and women.

The difference varies in different phases of life, from childhood to adolescence to adulthood. Males are more vulnerable to developing psychiatric disorders arising from insult to the central nervous system during ontogeny, probably because of a greater antigenicity to the pregnant mother. It has been suggested that this antigenicity may induce a state of maternal immunoreactivity which can lead, directly or indirectly, to fetal damage and thus to greater male susceptibility to environmental insults (Gualtieri & Hicks, 1995). Most studies show a higher prevalence of mental health problems in younger boys than in girls, the former experiencing more conduct disorders, with aggressive and antisocial behaviors. During adolescence the difference become smaller because girls experience more emotional problems, with fearful, anxious or overcontrolled behaviors. In adulthood men experience more alcohol and drug abuse and antisocial behavior, while women experience more anxiety, depression and eating disorders. Moreover, it is well known that males are much more likely to commit crimes (and more serious crimes) than women, as indicated by their higher arrest and imprisonment rates, and are more likely to commit suicide or to become homeless. Although there is no single cause of suicide, more than 90% of those who commit suicide have a
mental disorder and between a quarter and a half of single homeless men are suffering from severe mental disorder (Jorm, 1995).

The World Bank (1993) recently tabulated disability-adjusted life years. Depressive disorders account for almost 30% of the disability from neuropsychiatric disorders among women, but for only 12.6% among men. On the other hand, alcohol and drug dependence accounts for 31% of neuropsychiatric disability among men, but for only 7% of the disability among women. Desjarlais et al. (1995) reviewed 15 studies focusing on psychiatric disorders as well as on psychological distress, carried out over the last decades in many parts of the world, including Africa, Asia, the Middle East and Latin America, and stated that "comparative analysis of empirical studies of mental disorders reveals a consistency across diverse societies and social contexts: symptoms of depression and anxiety as well as unspecified psychiatric disorder and psychological distress are more prevalent among women, whereas substance use disorders are more prevalent among men". In other words "men tend to externalize their suffering through substance abuse and aggressive behavior, resulting in an under reporting of psychological distress. Women, in turn, more often suffer distress in the form of depression, anxiety, 'nerves', and the like" (Desjarlais et al., 1995, p.180).

Four questions need to be addressed at this point. First, what is the present "state of the art" with regard to the difference between men and women in the frequency of well-defined psychiatric disorders, when the literature is critically examined, paying attention to the main methodological factors and biases that may affect the results; and what are the differences when incidence and prevalence studies, as well as overall rates and rates of specific disorders are analyzed separately? Second, is the difference between men and women consistent when we move from the level of psychiatric disorders (including those considered more severe) to that of psychological distress and to the level of individual symptoms or complaints relating to (less severe) disorders? These various expressions of suffering, from the most severe psychiatric disorders to the individual symptoms or complaints, differ in many ways and are likely to be determined by different causes or to be influenced and shaped by different combinations of causal factors. For instance, a gradient of biological factors with a decreasing causal role, from the first to the last level, has been postulated. A difference between males and females in the rate and/or in the phenomenology and/or in the outcome of the condition under study, only at one level or at all levels of the spectrum, would have important theoretical and practical implications. Third, is a gender difference more likely to emerge when we use a longitudinal rather than a cross-sectional approach? Gender, for instance, may influence incidence of depression (females are more likely to make transition from subsyndromal to definite episode of depression) rather than course of illness and transition to recovery, while the contrary may be true for other disorders such as schizophrenia. Fourth, where a true difference has been convincingly proven we need to go a step further and try to answer another question: what factors account for the differences, or, in other words, why do men and women express their suffering in different ways and experience some symptoms and psychiatric disorders with different frequency?
Furthermore, what are the implications of these differences?

The present Monograph by Dr Marco Piccinelli and his co-worker, Dr. Gomez Homen is a well balanced and meticulous piece of work that will be found extremely useful by those attempting to reply to the first and, in part, to the second question (with reference to affective disorders and schizophrenia). It is also a worthwhile and informative starting point for answering questions three and four. It was a very demanding task to sort out and critically analyze the vast literature related to gender differences in affective disorders and schizophrenia. Other authors will hopefully extend this kind of analysis to other conditions and disorders. The third and fourth questions will need more attention in the future, not only from those collating critical reviews of the literature but also from those planning and designing research studies.

I would like to comment briefly on some aspects of each of the four questions listed above.

The first question (the present “state of the art” of the difference between men and women in the true rates of well-defined psychiatric disorders) is extensively addressed by the authors of this Monograph, with reference to the full spectrum of affective disorders and to schizophrenia. We should, however, put the results of their review of the literature in the context of studies concerning other disorders that they have not analyzed.

It has traditionally been believed that mental disorders are more common in females than in males. More recent evidence has shown that the picture is not so simple and that the difference concerns, as already mentioned, the patterns of disorders and not the overall prevalence. There are therefore differences in results between earlier and more recent studies (mainly general population surveys), due to the fact that earlier surveys concentrated on disorders which mostly affect females.

We must be very selective and critical in analyzing the vast amount of descriptive studies on gender differences in rates of psychiatric disorders and we must discard those that do not meet sufficiently high standards. The main methodological problems to be taken into account are sample size (with particular attention to non-response rates and refusal rates), confounding factors, and diagnostic reliability and validity. Moreover, many studies analyze one variable at a time for its relationships to mental disorder, failing to consider the possibility of multiple interactions among demographic variables (e.g. sex, marital status, employment) (Goldman & Ravid, 1980). For instance, Jablensky and Cole (1997) have recently published data from the extensive WHO-10 countries study of schizophrenia (778 males and 653 females). Applying a generalised linear modelling strategy they show that the gender difference in the age at onset of schizophrenia is not a robust biological characteristic of the disorder. A large part of the differences reported previously (males having an earlier onset) may well be explained by the failure to control for marital status and premorbid personality, when comparing the age of onset in the two sexes. The availability of mod-
ern statistical methods now make it possible to carry out more sophisticated, multivariate analyses and therefore to be more demanding in our selection of the literature, as well as in planning future studies.

The second question (are gender differences limited only to some psychiatric disorders, particularly the less severe, or do they consistently concern the full spectrum of sub-clinical and clinical conditions?) has not been tackled, to my knowledge, by any individual study. This is not surprising, considering that this would have to be a large community-based survey that should include large number of clinical cases. This is too difficult. The information we have is therefore derived from data taken from research carried out in different places at different times, sometimes with different methodologies. The general impression is that there is not a consistent continuum in gender differences from individual symptoms and complaints to the most severe psychiatric disorders. As far as affective disorders are concerned, it is reported in this Monograph that higher rates have been found in women than in men in studies of the prevalence of intermittent and brief recurrent depression, of dysthymia and of major depression, as well as (less convincingly) in studies of the incidence of depression, but not in studies of the prevalence or incidence of bipolar disorder. Further research which applies this “spectrum approach” is needed; these studies should use, across the spectrum, reliable and valid measures belonging to the same family of instruments and should analyze separately acute and chronic clinical conditions, paying attention to all well-defined subtypes of the disorders.

Differences may emerge only when we look specifically at particular subsyndromes. There is, in other words, a need to be more specific and more selective in future studies, in order to be able to detect gender-related differences that may otherwise be obscured, as well as in order to avoid the undue overestimation and generalization of overall differences.

For example, it is well known that, on the basis of gender differences reported in the literature, a two-syndrome model of schizophrenia has been postulated: an early onset, more chronic syndrome (primarily affecting men), and a later-onset, better prognosis syndrome (mainly affecting women). It is useful therefore to distinguish between these two forms instead of persisting in the study of schizophrenia as a unitary illness. In recent years, much attention has been directed toward the severe, early-onset form. It is now time to focus on the milder, later-onset form to which women appear particularly susceptible (Castle et al., 1995).

We need also to be more specific and more comprehensive in choosing the variables to be studied for the detection of sex differences. For example, neuroimaging studies of schizophrenia have accumulated in the literature over the last 20 years. However, as Vazquez-Barquero et al. (1995) have pointed out, the majority of these studies have not investigated the effect of sex on brain abnormalities.
The third question concerns the longitudinal approach in epidemiological psychiatry. This is increasingly being adopted, since we are increasingly moving from descriptive to outcome studies.

For example, in relation to affective disorders, the importance of adopting such an approach for studying gender influence in the transitions from asymptomatic to subsyndromal depression, to incident depression, to recovery or restitution and to relapse is intuitively clear. Does gender affect the transitions at the left side of the continuum or those at the right, or both? Patton et al. (1996) are actually carrying out a community-based multiwave cohort study of this kind in Australia. More longitudinal studies are clearly needed.

The fourth question (the question of causation and of implications of true gender differences) is a key question, or rather a key series of related questions.

Before discussing this point, I should like to stress that, in the literature, terms such as “sex”, “gender”, “sex-related” and “sex-linked” are often used inconsistently and/or interchangeably. This ambiguity is not just a semantic problem and the choice of the term used may reveal different attitudes and beliefs, as well as implicit assumptions about causality. The term “sex” often reflects a putative biological cause; “gender” a putative environmental (social, cultural, or political) cause of some reported difference. Sometimes (this is, I believe, the case for the authors of this Monograph) the term “sex” is used to refer to the biological aspect only, while “gender” relates to the complex interaction between biological, psychological and social variables. The issue has been widely discussed in the field of normal psychology, but has surprisingly been forgotten or understated in psychopathology where the implications of a semantic misuse may be greater.

As Lewine (1994) pointed out in relation to the study of schizophrenia, a simple distinction between the two terms, without any assumptions about etiology, is the more useful approach. The term “sex” should therefore be used in reference to comparisons based on the demographic categories of female and male, while the term “gender” in reference to comparisons of femaleness and maleness, of masculinity and femininity, as suggested by Deaux (1993). The results of a study by Daniel et al. (1988) may illustrate the usefulness of this distinction: using PET scanning they found a higher rate of cerebral blood flow in healthy women than in healthy men. However, when classified according to the femininity/masculinity score, subjects who had high femininity (both women and men) had higher blood flow than subjects with low femininity score. The difference was therefore related more to gender than to sex.

According to the approach mentioned above, most research on mental symptoms and mental disorders could be defined as “sex” research. It is easier and more straightforward, especially in large epidemiological surveys, to simply classify subjects according to the demographic category they
belong to. The interpretation of the results will depend on the relative weight that each of the biological/psychological/social components may have. These relative weights are often unknown and may only be inferred. In future research the formal assessment of femininity and masculinity, as well as of social role, and economic, political and social status, could be useful for attempting to dissect and take into account separately the weight of each of the three different components. The results of the study on sex differences in the prevalence of minor psychiatric morbidity completed by Jenkins (1985) is exemplary in this respect: if samples of male and female subjects are chosen who are closely comparable from the standpoint of social adjustment, the sex difference completely disappears.

We are in the difficult situation of trying to use gender, “an immutable sociodemographic variable”, as a tool to understand etiologic or risk factors of mental disorders, without knowing the relative weight of the various biological and psychosocial factors that make a woman different from a man (and vice versa). On one side there are clear-cut biological factors (for example, the endocrine factors), while on the other side, there are factors related to roles, stereotypes and social circumstances. What really matters?

The answer cannot be straightforward, for many reasons, including the relevance of the interactions between biological, psychological and social factors. For instance, Freud (1905/1953) hypothesized that hormonal changes cause sexual instinctual transformations at puberty as well as the formation of defense mechanisms used to combat these overwhelming libidinal drives. Moreover, we should consider that the sex stereotype belief system has evolved to rationalize the biological difference between the genders and to provide as socialization models (Lieh Mak, 1994).

On the other hand it is helpful to think of two main groups of causes of mental disorders: physical and biological on one hand (genetic component, birth trauma, maternal infections at a particular point in a pregnancy), and on the other hand social, situational and interactional (stressful factors as well as buffers to diminish the impact of unfavorable external events). Again it is not possible to be precise about the relative importance of the biological/physical and social/cultural sets of factors in contributing to mental disorder. The sex/gender variable, as underlined above, contains both types of factors, so a multidimensional and interactive approach needs to be taken.

A large WHO study, carried out in general health care settings, adopted a cross-cultural approach for attempting to evaluate the relative influence on sex differences of biological and social factors (Gater et al., 1996). Prevalence rates of common mental disorders in men and women were assessed using a two-stage design from 26,969 primary care attenders in 15 centres in four continents, including Verona, Italy. The same standardized methods were used across different centres and cultures. Logistic regression analysis was used to test whether sex differences were consistent across centres. We found that the absence of a sex by centre effect for current depression and
agoraphobia or panic disorder was consistent with biological or psycho-social factors, either interacting or working alone, that have a similar final time effect across cultures. It did not support the idea that sex differences in prevalence are caused by local psycho-social factors that vary from country to country. On the other hand, the variation in odds ratio for generalized anxiety disorder suggested that there are differences between the centres that contribute to the sex difference in rates for this disorder. These were most likely to be related to sociocultural differences between the social roles and experiences of women and men.

Little investigation has been carried out until now on the different ways men and women may respond to the same stressful events. This approach could be useful to remove some of the obstacles to progress in clarifying the complex issue of causation of gender differences.

Najman (1995) reports the results of an interesting 30-month longitudinal study by Boyle (1994) on the impact of one specific stressful event - the death of a child - on the mental health of the parents. Mental health was also measured in control parents. It was shown that men and women respond differently to the same events and that the ways this response is measured determines which group is perceived to have the highest rate of mental disorders. When excessive alcohol consumption is excluded as a criterion of mental disorder, mothers have higher rates, regardless of whether they were bereaved. When a high level of alcohol use is included, these previous differences diminish or are eliminated in all groups of parents except those most recently bereaved.

Desjarlais et al. (1995, p. 183)), after reviewing the proposed explanations of observed gender differences in psychiatric morbidity which “taken together, illuminate the quality of women's lives”, conclude that “poverty, domestic isolation, powerlessness (resulting, for example, from low levels of education and economic dependence) and patriarchal oppression, are all associated with higher prevalence of psychiatric morbidity (exclusive of substance disorder) in women. In short, a considerable body of evidence points to the social origins of psychological distress for women”. In their book they underline that the explanations proposed for gender differences in psychiatric morbidity in Asia, Africa, the Middle East and Latin America “echo established associations among poverty, isolation, and psychiatric morbidity for women in Western Europe and the United States” (see Dennerstein et al., 1993). To support the latter statement they quote many studies: a classic research study which found depression to be more prevalent among working-class than middle-class women living in London (Brown & Harris, 1978); studies which reported poor women experiencing more and more severe life events than the general population (Brown et al., 1965; Makosky, 1982); studies reporting that poor women are more likely to have to deal with chronic sources of social stress in the form of low-quality housing or dangerous neighbourhoods (Makosky, 1982); research showing women at higher risk for becoming victims of violence (Belle, 1990); and studies indicating that women are especially vulnerable in encountering problems in parenting and child care (Belle et al., 1988). So, what really matters?
As the authors of this Monograph say in their introduction, “the incorporation of a gender-related perspective into psychiatric research may have important implications for clinical practice, public health policy and theory”. I have discussed already the implications for theory, which cannot be separated from issues related to causation. I should like to give now some thought to the other two implications.

Some of the implications for public health policy of higher rates of emotional distress, anxiety and depressive disorders in women, are summarized by the recommendations of the 1991 National Council for International Health’s (NCIH) Conference in Women’s Health, which take a world perspective. They read as follows: 1) establishing baselines for women’s health and well-being and then measuring progress toward those standards; 2) developing ways of monitoring the impact of structural adjustment programmes on women’s welfare and establishing programmes to mitigate their adverse effects; 3) enforcing or enacting legislation to improve women’s status; 4) addressing women’s need for equitable employment and economic development; and 5) expanding education for women and girls (Jacobson, 1993). We could add that an increase in the investment for research and service provision to improve psychological well-being, and to reduce rates of alcohol abuse, aggression and suicide in men are also necessary and will also indirectly address the needs of their wives and children.

Finally, the clinical implications. There is no doubt that the clinician would benefit from increased knowledge of gender-specific factors that may predict and influence the phenomenology, course and outcome of mental disorders. Even if we need more hard data before this hope can become reality, encouraging results are appearing on the horizon. On the biological side, for instance, the psychotropic potential of oestrogens in schizophrenic women before and after the menopause and the hypothesis to adjust, in young fertile women, the neuroleptic dosage to the menstrual cycle are examples of encouraging implications for future clinical practice.

What can we do in the meantime in our daily clinical practice, while waiting for more hard data from research to be translated into the care and treatment of individual patients? Communication among physicians and other health workers and women patients is paternalistic in many parts of the world. As Dejarlais et al. (1995) report, “Women are often neither encouraged not permitted to voice their feelings and complaints. When they do, they are likely to be discounted or dismissed.” The results of studies on gender differences in mental disorders may have immediate training implications: “health care professionals must be trained to empower women in the clinical encounter”.

In the next decade, we should see to what extent sound research will provide answers to the four questions listed above and will be able to increase our knowledge and improve prevention, care and treatment of psychological suffering and psychiatric disorders both in women and in men.
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INTRODUCTION

Epidemiologic research in the field of psychiatry has shown that gender is a crucial variable influencing the distribution and features of mental disorders. Thus, the incorporation of a gender-related perspective into psychiatric research may have important implications for clinical practice, public health policy and theory. On a clinical ground, since gender can be considered an ‘immutable sociodemographic variable’ that cannot be influenced by the disease, it would be useful to identify gender-specific factors that may influence and predict symptom patterns, co-morbidity, course, outcome and response to treatment. From the public health perspective, gender differences in rates of a disorder and its characteristics may help to understand the health needs and treatment expectations of a population, to set the techniques for the monitoring of the health of a population, to plan treatment decisions and health services, to allocate the existing resources or to search for new resources. Theoretically, since gender is a proxy for a complex of psychosocial and biological variables, much can be known about specific etiologic or risk factors that underlie the association, interactions or processes by which vulnerability progresses into clinical disorders (Goodwin & Blehar, 1993).

The aim of this work is to report the main epidemiologic findings on gender differences in affective disorders and schizophrenia. In addition, methodologic difficulties that might bias research findings and be artifactual determinants of gender differences are discussed. Finally, the main factors that can best explain the gender differences in affective disorders and schizophrenia will be outlined as suggested by different theoretical approaches.
METHOD

Papers were collected using four strategies. First, the Medline data base was searched for the years 1985 to January 1995, using the keyword 'mental disorders' matched with any of the following in the title or abstract: 'sex', 'gender', 'male', 'female', 'men', 'women', 'boys', and 'girls'. This search was originally aimed at locating papers on gender differences in any type of mental disorders, not only in affective disorders and schizophrenia. Thus, we integrated this search by consulting the Medline CD ROM database for the period 1985 to May 1996, using the keywords 'schizophrenia', 'affective disorder', 'bipolar disorder', 'manic disorder', 'depressive disorder', 'mania', 'depression' and 'dysthymia' matched with the keywords 'sex' and 'gender' in the title or abstract. Second, literature was supplemented by hand-searching psychiatric journals and by consulting recent published reviews and bibliographies. Third, secondary references were identified by examining the reference sections of the papers located with the methods listed above. Finally, seven renowned experts in the field (see Acknowledgements) were contacted by mail and asked to select the most relevant papers recently published on gender differences in affective disorders and schizophrenia.
AFFECTIVE DISORDERS

INTRODUCTION

A wide variety of principles and criteria are being used in the assessment and classification of affective disorders. For example, Angold (1988) has suggested that at least eight distinctions can be made in the use of the term ‘depression’, some of which consider ‘depression’ as referring to a single item or state or trait and others refer to a mood state plus its biological, cognitive and/or behavioural concomitants. Similarly, Farmer & McGuffin (1989) have reviewed the ‘contemporary confusion’ surrounding the classification of depression and noted how the approaches advocated by nosologists varied considerably, some subdividing depression into one or two subtypes, while others proposing multiple different categories. Although different diagnostic concepts may serve specific research or clinical purposes, few of them have been sufficiently explored and validated (Jablensky, 1987). Indeed, research in the field of affective disorders faces specific methodological difficulties. Since biological or trait markers are relatively few and of unclear specificity, they are of little help in the identification of homogeneous diagnostic subtypes. Moreover, given the dimensional nature of much psychiatric morbidity and the absence of rarity points or interruptions in the symptom distribution, the definition of psychiatric ‘caseness’ is often arbitrary (Kendell, 1988). In light of these limitations, we have decided to present findings according to well-known systems for classifying mental disorders (e.g., the Research Diagnostic Criteria, the International Classification of Diseases, and the Diagnostic and Statistical Manual of Mental Disorders), since they have tried to reduce heterogeneity of diagnostic categories and limit criterion variance to an acceptable degree.

Although several forms of affective disorders have been investigated and described, epidemiologic evidence pertains mainly to bipolar disorder and major depression. Thus, these disorders are the main focus of the present work. In addition, epidemiologic findings on dysthymia (DSM-III - APA, 1980 - and DSM-III-R - APA, 1987), intermittent depression (Research Diagnostic Criteria - Spitzer et al., 1978) and brief recurrent depression (ICD-10 - WHO, 1992) are presented together under the heading ‘persistent and recurrent depression’. A detailed review of similarities and differences between these diagnostic categories has been recently published after a working party of renowned experts summoned by the World Psychiatric Association (Costa e Silva & Freeman, 1994).

In the present work, epidemiologic findings are reported on gender differences in affective disorders among the adults, since published research suggests that gender differences are limited or even absent in either childhood or old age (Jorm, 1987; Burvill, 1995). Possible reasons for this age-related effect will be discussed alongside with the factors accounting for gender differences in affective disorders.
PREVALENCE OF MAJOR DEPRESSION

Current prevalence rates

Table I sets out the results of general population studies investigating current prevalence rates of major depression by sex of respondents. Current major depression was defined as criteria for major depression being fulfilled at the time of the examination or during the previous month.

Three studies were carried out in the United States. Weissman & Myers (1978) reported rates of affective disorders from the first epidemiologic survey applying Research Diagnostic Criteria to a community sample; the findings refer to a 1975 follow-up of a probability sample initially selected and studied in 1967. Prevalence estimates reported by Regier et al. (1993) were derived from the NIMH-Epidemiologic Catchment Area Study, a large-scale survey in which five sites geographically distributed throughout the United States were each randomly sampled to yield an estimate of rates of psychiatric disorders among noninstitutionalized adults aged 18 years and older. Finally, Blazer et al. (1994) presented one-month prevalence rates of major depression from the National Comorbidity Survey, in which a structured psychiatric interview was administered to a representative national sample of community residents in the United States aged 15 to 54 years. Although direct comparison between these studies is limited by a number of methodological factors (including differences in research instruments, diagnostic criteria, age range and size of the samples), a common finding was that rates of major depression were higher among females, with a female-to-male sex ratio ranging between 1.6 and 1.8.

In Florence, Italy, Faravelli et al. (1990) reported the highest female-to-male sex ratio (3.2) in a sample of subjects randomly selected from the lists of seven primary care physicians with postgraduate training in psychiatry; respondents were interviewed by primary care physicians, using a flow-chart that included the hierarchical system of diagnosis for affective disorders drawn from DSM-III.

Females were at increased risk for major depression compared to males also in Hollifield et al.’s (1990) study, in which a random sample of the families living in a small lowland town in Leshoto was examined. Moreover, when rates of current psychiatric disorders were corrected for gender and for alcohol abuse (due to a higher proportion of males being missed at interview and a sizeable proportion of individuals with major depression abusing alcohol), the same female-to-male sex ratio (1.6) was found, estimated rates for major depression being 7.1% in males and 11.7% in females.

Finally, Stefánsson et al. (1994) investigated rates of psychiatric disorders in a cohort of subjects including half of the population born in Iceland in 1931 and living there on December 1986.
Table I - Current prevalence rates of major depression from general population studies

<table>
<thead>
<tr>
<th>Author Country, time</th>
<th>Sample (N)</th>
<th>Age range (years)</th>
<th>Instruments Diagnostic Criteria</th>
<th>Rates (%) Males Females Total</th>
<th>Female-to-Male Sex Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weissman &amp; Myers (1978)* USA, 1975-76</td>
<td>511</td>
<td>26 and over</td>
<td>SADS RDC</td>
<td>3.2 5.2 4.3 1.6 : 1</td>
<td></td>
</tr>
<tr>
<td>Regier et al. (1993)** USA, 1980-83</td>
<td>18,571</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>1.6 2.9 2.2 1.8 : 1</td>
<td></td>
</tr>
<tr>
<td>Blazer et al. (1994)** USA, 1990-92</td>
<td>8,098</td>
<td>15 - 54</td>
<td>CIDI DSM-III-R</td>
<td>3.8 5.9 4.9 1.6 : 1</td>
<td></td>
</tr>
<tr>
<td>Faravelli et al. (1990)* Italy, 1984</td>
<td>1,000</td>
<td>15 and over</td>
<td>Flow chart DSM-III</td>
<td>1.3 4.1 2.8 3.2 : 1</td>
<td></td>
</tr>
<tr>
<td>Hollifield et al. (1990)** Leshoto, 1986-1987</td>
<td>356</td>
<td>19 - 93</td>
<td>DIS DSM-III</td>
<td>8.8 14.5 12.4 1.6 : 1</td>
<td></td>
</tr>
<tr>
<td>Stefansson et al. (1994)** Iceland, 1987-88</td>
<td>862</td>
<td>55-57</td>
<td>DIS DSM-III</td>
<td>0.9a 2.9a 1.9a 3.2 : 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.5b 0.5b 0.5b 1.0 : 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.7c 1.7c 1.2c 2.4 : 1</td>
<td></td>
</tr>
</tbody>
</table>

* Major depression present at interview
** 1-month prevalence rates for major depression
a Major depressive episode (total)
# Major depression, single episode
c Major depression, recurrent

Rates of major depression were low compared to the other studies. The preponderance of major depression among females was accounted for by recurrent major depression, whereas a female-to-male sex ratio equal to 1.0 was obtained for subjects suffering from a single episode of major depression over the month preceding the examination.

For comparison, Table II shows the results of studies which investigated rates of depressive disorders in the general population, using the Present State Examination. The Present State Examination is a semistructured psychiatric interview for eliciting and rating psychiatric symptoms present during the month preceding the evaluation; the interview is supplemented by a computer program (CATEGO), which allows the allocation of patients into classes according to their current symptoms (Wing & Sturt, 1978). The decision to consider these studies separately was based on two reasons. First, the Present State Examination by itself does not generate diagnoses, although it provides a symptom profile that allows the approximate allocation of patients into one of the ICD-
Table II - One-month prevalence rates of depressive disorders according to PSE-ID-CATEG0 and ICD-8

<table>
<thead>
<tr>
<th>Author Country, time</th>
<th>Sample (N)</th>
<th>Age range (years)</th>
<th>Rates (%)</th>
<th>Female-to-Male Sex Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orley &amp; Wing (1979) Uganda, 1972</td>
<td>206</td>
<td>18 - 65</td>
<td>14.3\textsuperscript{a} 22.6\textsuperscript{a}</td>
<td>—</td>
</tr>
<tr>
<td>Henderson et al. (1979) Australia, 1977</td>
<td>756</td>
<td>18 and over</td>
<td>2.6\textsuperscript{b} 6.7\textsuperscript{b}</td>
<td>—</td>
</tr>
<tr>
<td>Bebbington et al. (1981) UK, n.r.</td>
<td>310</td>
<td>18-64</td>
<td>4.8\textsuperscript{b} 9.0\textsuperscript{b} 7.0\textsuperscript{b}</td>
<td>—</td>
</tr>
<tr>
<td>Mavreas et al. (1986) Greece, n.r.</td>
<td>489</td>
<td>18-74</td>
<td>4.3\textsuperscript{b} 10.1\textsuperscript{b} 7.4\textsuperscript{b}</td>
<td>—</td>
</tr>
<tr>
<td>Mavreas &amp; Bebbington (1987) UK*, n.r.</td>
<td>219</td>
<td>18-64</td>
<td>4.1\textsuperscript{b} 7.0\textsuperscript{b} 5.5\textsuperscript{b}</td>
<td>—</td>
</tr>
<tr>
<td>Lethinen et al. (1990) Finland, 1985-87</td>
<td>747</td>
<td>30-80</td>
<td>2.4\textsuperscript{b} 6.5\textsuperscript{b} 4.6\textsuperscript{b}</td>
<td>—</td>
</tr>
</tbody>
</table>

\* Study conducted among Greek Cypriot immigrants in London
\textsuperscript{a} Depressive disorders not otherwise specified
\textsuperscript{b} Including ICD-8 categories 296.2 (manic-depressive psychosis, depressed type) and 300.4 (depressive neurosis)

n.r. = not reported

8 categories. Second, the investigators using the Present State Examination in surveys of the general population reported overall prevalence rates of depressive disorders without distinction between ‘depressive neurosis (300.4)’ and ‘manic-depressive psychosis, depressed type (296.2)’, whereas recent epidemiologic findings on sex and age distribution of bipolar disorder, major depression and dysthymia support the separation of bipolar disorder from other types of affective disorders (Weissman et al., 1988). As a result of differences in geographical location, survey designs and socio-demographic characteristics of populations where surveys were carried out, only gross comparisons can be made among these studies. In spite of these limitations, all the studies pointed to a preponderance of depressive disorders among females, with a female-to-male sex ratio ranging between 1.6 and 2.7.

**Six-month prevalence rates**

Table III sets out the results of general population studies investigating six-month prevalence rates of major depression by sex of respondents. The six-month prevalence rates reported here
included those subjects who met lifetime criteria for major depression and experienced relevant symptoms or an episode of the disorder during the six months preceding the examination.

Six studies used the Diagnostic Interview Schedule, a structured psychiatric interview designed for administration by lay interviewers in large-scale epidemiologic surveys to detect psychiatric disorders according to the DSM-III criteria. Four of these studies relied on a two-stage probability sample design: at the first stage, households were systematically sampled from lists of residential addresses; at the second stage, a listing of residents was obtained for each sample household and one household member was randomly selected among those eligible. Canino et al. (1987) selected individuals living in households throughout Puerto Rico as well as household members temporarily away and those in institutions. Bland et al. (1988a) examined a sample of community residents in Edmonton, Canada, aged 18 years and older in addition to a systematic sample of residents in a nursing home/auxiliary hospital group; the findings presented here refer to the noninstitutionalized individuals only. In New Zealand, Oakley-Browne et al. (1989) selected household members aged 18 to 64 years resident in the Christchurch Urban Area, including the city itself, suburbs and the semi-rural margins. Since affective disorders and eating disorders were of particular interest, females aged 18 to 44 years were oversampled to increase the yield of these disorders. In France, Lepine et al. (1989) conducted their survey in Savigny, a newly built town located near Paris. The rates of major depression in Christchurch were clearly higher than at the other three sites; there was a predominance of females as compared to males in the rates of major depression at all sites, with a female-to-male sex ratio ranging between 1.3 and 2.4.

Higher rates of major depression among females were also found in the other two studies using the Diagnostic Interview Schedule and DSM-III criteria. In the National Survey of Deviant Behavior conducted in the United States only young adults aged 18 to 24 years were assessed for psychiatric status (Elliott et al., 1985). In the Icelandic sample studied by Stefánsson et al. (1994) recurrent major depression was responsible for the predominance of females in the overall rates of major depression, whereas the two sexes did not differ in reporting a single episode of major depression.

Finally, Levav et al. (1993) selected a probability sample of first generation Jewish Israelis of either European or North-African parents using a two-stage design, in which final diagnoses were made by psychiatrists on the basis of the Schedule for Affective Disorders and Schizophrenia-Research Diagnostic Criteria. The female-to-male sex ratio for major depression was slightly greater than 1.0 when major depression was assessed both at the probable and at the definite level of diagnostic confidence.
### Table III - Six-month prevalence rates of major depression from general population studies

<table>
<thead>
<tr>
<th>Author and Country, time</th>
<th>Sample (N)</th>
<th>Age range (years)</th>
<th>Instruments Diagnostic Criteria</th>
<th>Rates (%) Males</th>
<th>Rates (%) Females</th>
<th>Rates (%) Total</th>
<th>Female-to-Male Sex Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canino et al. (1987) Puerto Rico, 1984</td>
<td>1,513</td>
<td>18 - 64</td>
<td>DIS DSM-III</td>
<td>2.4</td>
<td>3.3</td>
<td>3.0</td>
<td>1.3 : 1</td>
</tr>
<tr>
<td>Bland et al. (1988a) Canada, 1983-86</td>
<td>3,258</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>2.5</td>
<td>3.9</td>
<td>3.2</td>
<td>1.6 : 1</td>
</tr>
<tr>
<td>Oakley-Browne et al. (1989) New Zealand, 1986</td>
<td>1,498</td>
<td>18-64</td>
<td>DIS DSM-III</td>
<td>3.4</td>
<td>7.1</td>
<td>5.3</td>
<td>2.1 : 1</td>
</tr>
<tr>
<td>Lepine et al. (1989) France, n.r.</td>
<td>749</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>1.5</td>
<td>3.6</td>
<td>—</td>
<td>2.4 : 1</td>
</tr>
<tr>
<td>Elliott et al. (1985) USA, 1983</td>
<td>1,496</td>
<td>18 - 24</td>
<td>DIS DSM - III</td>
<td>3.1*</td>
<td>8.0*</td>
<td>5.5*</td>
<td>2.6 : 1</td>
</tr>
<tr>
<td>Stefansson et al. (1994) Iceland, 1987-88</td>
<td>862</td>
<td>55 - 57</td>
<td>DIS DSM-III</td>
<td>1.1a</td>
<td>3.6a</td>
<td>2.3a</td>
<td>3.3 : 1</td>
</tr>
<tr>
<td>Levav et al. (1993) Israel, 1982-88</td>
<td>2,741</td>
<td>24 - 33</td>
<td>SADS RDC</td>
<td>3.8d</td>
<td>4.5d</td>
<td>4.2d</td>
<td>1.2 : 1</td>
</tr>
</tbody>
</table>

* Data derived from Weissman et al. (1988)

- a Major depressive episode (total)
- b Major depression, single episode
- c Major depression, recurrent
- d Either probable or definite level of diagnostic accuracy
- e Only definite level of diagnostic accuracy

- n.r. = not reported

### Twelve-month prevalence rates

Table IV sets out the results of general population studies investigating 12-month prevalence rates of major depression by sex of respondents. The 12-month prevalence rates reported here included those subjects who met lifetime criteria for major depression and had experienced relevant symptoms or an episode of the disorder during the 12 months preceding the examination.

In five studies, rates of major depression were expressed according to the DSM-III criteria. In the United States, the nationwide survey carried out by Uhlenhuth et al. (1983) primarily to determine the prevalence and patterns of psychotropic drug prescriptions and the NIMH-Epidemiologic Catchment Area Study (Robins & Regier, 1991) were based on a stratified multistage probability
sample of subjects in the noninstitutionalized civilian population. In Florence, Italy, Faravelli et al. (1990) selected a random sample of the general population from the lists of primary care physicians. Ernst & Angst (1992) selected a cohort of young males and females from the Kanton Zürich in Switzerland, who were born in 1957 and 1958. Finally, Stefánsson et al. (1994) selected half of the population born in Iceland in 1931.

On the other hand, prevalence rates of major depression were expressed according to the DSM-III-R criteria in the survey conducted in Savigny, France (Lepine et al., 1993) and in the National Comorbidity Survey in the United States (Kessler et al., 1994).

Despite wide variation in rates of major depression across the studies (between 2.7% and 10.3%), rates were higher in females compared to males and this trend was consistent across all the studies, with a female-to-male sex ratio ranging between 1.7 and 2.9.

<p>| Table IV - Twelve-month prevalence rates of major depression from general population studies |
|---------------------------------------------------------------|-------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Author Country, time</th>
<th>Sample (N)</th>
<th>Age range (years)</th>
<th>Instruments Diagnostic Criteria</th>
<th>Rates (%)</th>
<th>Total</th>
<th>Female-to-Male Sex Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uhlenhuth et al. (1983) USA, 1979</td>
<td>3,161</td>
<td>18 - 79</td>
<td>Symptom checklist DSM - III</td>
<td>2.8</td>
<td>5.1</td>
<td>2.5 : 1</td>
</tr>
<tr>
<td>Robins &amp; Regier (1991) USA, 1980-83</td>
<td>18,571</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>1.4</td>
<td>2.7</td>
<td>2.9 : 1</td>
</tr>
<tr>
<td>Faravelli et al. (1990) Italy, 1984</td>
<td>1,000</td>
<td>15 and over</td>
<td>Flow chart DSM-III</td>
<td>3.5</td>
<td>6.3</td>
<td>2.5 : 1</td>
</tr>
<tr>
<td>Ernst &amp; Angst (1992) Switzerland, 1979</td>
<td>591</td>
<td>20 - 21</td>
<td>Semistructured interview DSM-III</td>
<td>4.8</td>
<td>10.8</td>
<td>2.3 : 1</td>
</tr>
<tr>
<td>Stefansson et al. (1994) Iceland, 1987-88</td>
<td>862</td>
<td>55 - 57</td>
<td>DIS DSM-III</td>
<td>1.8a</td>
<td>2.9a</td>
<td>2.2 : 1</td>
</tr>
<tr>
<td>Lepine et al. (1993) France, n.r.</td>
<td>1,746</td>
<td>18 and over</td>
<td>DIS DSM-III-R</td>
<td>3.4</td>
<td>6.0</td>
<td>1.8 : 1</td>
</tr>
<tr>
<td>Kessler et al. (1994) USA, 1990-92</td>
<td>8,098</td>
<td>15 - 54</td>
<td>CIDI DSM-III-R</td>
<td>7.7</td>
<td>12.9</td>
<td>1.7 : 1</td>
</tr>
</tbody>
</table>

\[a\] Major depressive episode (total)

\[b\] Major depression, single episode

\[c\] Major depression, recurrent

*n.r. = not reported*
Lifetime prevalence rates

Table V sets out the results of general population studies investigating lifetime prevalence rates of major depression by sex of respondents. The lifetime prevalence rates of major depression reported here included those subjects who ever met the criteria for the disorder during the entire lifespan prior to the examination.

Nine studies used the Diagnostic Interview Schedule and DSM-III criteria. The surveys carried out in Puerto Rico (Canino et al., 1987), Edmonton (Bland et al., 1988a) and Christchurch (Wells et al., 1989) and the NIMH-Epidemiologic Catchment Area Study (Robins & Regier, 1991) were based on household probability samples, with estimated rates for major depression being obtained by weighing the collected data to correct for the selection procedure. The studies carried out in Savigny (Lepine et al., 1989) and in Iceland (Stefánsson et al., 1991) were drawn as random samples and, thus, the weighting procedure was not required. The Taiwan Psychiatric Epidemiology Project sampled three populations in metropolitan, township and rural areas, using a multistage random sampling method that did not create skewed sampling weights in a specific sampling area (Hwu et al., 1989). The Korean Epidemiologic Study of Mental Disorders was a nationwide survey including households in Seoul and in rural locations scattered over the country; in each household all family members aged 18 to 65 years were interviewed, provided that they had lived there for more than three months (Lee et al., 1990a, b). The Münich Follow-up Study (Wittchen et al., 1992) was a seven-year prospective and retrospective follow-up investigation of a stratified random sample of the general population of former West Germany; the stratification method used at follow-up included all the individuals reporting high scores on the clinical rating scales at the baseline evaluation plus a 39.8% random sample of those with low scores. Finally, the Shatin Community Mental Health Survey randomly selected households in Hong Kong, with one member between 18 and 64 years of age being randomly interviewed from each selected household (Chen et al., 1993). The lifetime rates of major depression varied widely by site, ranging between 3.3% and 16.8%. However, there was a predominance of females as compared to males in the rates of major depression at all sites, with a female-to-male sex ratio ranging between 1.4 and 3.4.

Two studies were based on different research instruments and diagnostic criteria. Weissman & Myers (1978) relied on the Schedule for Affective Disorders and Schizophrenia-Research Diagnostic Criteria. Kessler et al. (1994) used the Composite International Diagnostic Interview, a structured interview that was derived from the Diagnostic Interview Schedule and generates diagnoses according to the DSM-III-R criteria. Both studies showed a predominance of females as compared to males in the rates of major depression.

In Table V are also reported (when available) the female-to-male sex ratios resulting from rates of major depression at each site being standardized to the Epidemiologic Catchment Area five site household sample. This work was undertaken by the Cross National Collaborative Group, formed in 1990 by investigators having epidemiologic community data based on the Diagnostic Interview
<table>
<thead>
<tr>
<th>Author</th>
<th>Sample (N)</th>
<th>Age range (years)</th>
<th>Instruments Diagnostic Criteria</th>
<th>Rates (%)</th>
<th>Female-to-Male Sex Ratio</th>
<th>Female-to-Male Sex Ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canino et al. (1987) Puerto Rico, 1984</td>
<td>1,513</td>
<td>18 - 64</td>
<td>DIS DSM-III</td>
<td>Males: 3.5 Females: 5.5 Total: 4.6</td>
<td>1.8 : 1</td>
<td>1.8 : 1</td>
</tr>
<tr>
<td>Bland et al. (1988b) Canada, 1983-86</td>
<td>3,258</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>Males: 5.9 Females: 11.4 Total: 8.6</td>
<td>1.9 : 1</td>
<td>1.9 : 1</td>
</tr>
<tr>
<td>Wells et al. (1989) New Zealand, 1986</td>
<td>1,498</td>
<td>18 - 64</td>
<td>DIS DSM-III</td>
<td>Males: 8.8 Females: 16.3 Total: 12.6</td>
<td>1.9 : 1</td>
<td>2.1 : 1</td>
</tr>
<tr>
<td>Robins &amp; Regier (1991) USA, 1980-83</td>
<td>18,571</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>Males: 2.6 Females: 7.0 Total: 4.9</td>
<td>2.7 : 1</td>
<td>2.6 : 1</td>
</tr>
<tr>
<td>Lepine et al. (1983) France, n.r.</td>
<td>749</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>Males: 8.5 Females: 21.9 Total: —</td>
<td>2.8 : 1</td>
<td>2.1 : 1</td>
</tr>
<tr>
<td>Stefansson et al. (1991) Iceland, 1987-88</td>
<td>862</td>
<td>55 - 57</td>
<td>DIS DSM-III</td>
<td>Males: 2.9 Females: 7.8 Total: 5.3</td>
<td>2.7 : 1</td>
<td>—</td>
</tr>
<tr>
<td>Hwu et al. (1989) Taiwan, 1982-85</td>
<td>11,004</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>Males: 7.3 Females: 10.2 Total: 8.6</td>
<td>1.4 : 1</td>
<td>1.6 : 1 (total sample)</td>
</tr>
<tr>
<td>Lee et al. (1990a,b) Korea, n.r.</td>
<td>3,134</td>
<td>18 - 65</td>
<td>DIS DSM-III</td>
<td>Males: 2.4 Females: 4.1 Total: 3.3</td>
<td>1.7 : 1</td>
<td>2.0 : 1 (total sample)</td>
</tr>
<tr>
<td>Wittchen et al. (1992) Germany, 1981</td>
<td>483</td>
<td>25 - 64</td>
<td>DIS DSM-III</td>
<td>Males: 4.0 Females: 13.6 Total: 9.0</td>
<td>3.4 : 1</td>
<td>3.5 : 1</td>
</tr>
<tr>
<td>Chen et al. (1993) Hong Kong, 1984-86</td>
<td>7,229</td>
<td>18 - 64</td>
<td>DIS DSM-III</td>
<td>Males: 1.3 Females: 2.4 Total: —</td>
<td>1.9 : 1</td>
<td>—</td>
</tr>
<tr>
<td>Weissman &amp; Myers (1978) USA, 1975-76</td>
<td>511</td>
<td>26 and over</td>
<td>SADS RDC</td>
<td>Males: 12.3 Females: 25.8 Total: 20.0</td>
<td>2.1 : 1</td>
<td>—</td>
</tr>
<tr>
<td>Kessler et al. (1994) USA, 1990-92</td>
<td>8,098</td>
<td>15 - 54</td>
<td>CIDI DSM-III-R</td>
<td>Males: 12.7 Females: 21.3 Total: 17.1</td>
<td>1.6 : 1</td>
<td>—</td>
</tr>
</tbody>
</table>

* Rates of major depression at each site were standardized to the Epidemiologic Catchment Area five site household sample for the age group 18-64 years

a Major depressive episode (total)
b Major depression, single episode
c Major depression, recurrent
d Metropolitan Taipei
e Small towns
f Rural villages
g Urban area
h Rural area
n.r. = not reported
Schedule and DSM-III criteria, in order to analyze the data and compare the findings using a common data plan and the same definitions (Weissman et al., 1993). The Epidemiologic Catchment Area Study was designated as the reference sample since it had the largest sample size and a sampling scheme robust enough to ensure stability of findings. Prevalence rates standardized in this way produced estimates as if the population at each site had the same sex and age distribution of the Epidemiologic Catchment Area Study sample. Since the age ranges sampled at each site differed, analyses were limited to individuals aged 18 to 64 years. Females retained their predominance over males in rates of major depression at all sites, the female-to-male sex ratio ranging between 1.6 and 2.6.

**PREVALENCE OF PERSISTENT AND RECURRENT DEPRESSION**

Table VI sets out the results of general population studies investigating lifetime prevalence rates of dysthymia by sex of respondents.

Nine studies used the Diagnostic Interview Schedule and DSM-III criteria; since dysthymia is a chronic disorder, the Diagnostic Interview Schedule does not attempt to define onset or remission and only lifetime rates of the disorder are assessed. The surveys carried out in Puerto Rico (Canino et al., 1987), Edmonton (Bland et al., 1988b), Christchurch (Wells et al., 1989), Korea (Lee et al., 1990a, b), the United States (Robins & Regier, 1991) and Hong Kong (Chen et al., 1993) were based on household probability samples of the general population. The Taiwan Psychiatric Epidemiology Project sampled three populations in metropolitan, township and rural areas (Hwu et al., 1989). The study carried out in Iceland (Stefánsson et al., 1991) included half of the population born in Iceland in 1931 and living there in December 1986. Finally, the Münich Follow-up Study (Wittchen et al., 1992) was a seven-year prospective and retrospective follow-up investigation of a stratified random sample of the general population of former West Germany. The lifetime rates of dysthymia varied widely by site, ranging between 1.9% and 15.1%. There was a predominance of females as compared to males in the rates for dysthymia at all sites, with a female-to-male sex ratio ranging between 1.2 and 4.8.

On the other hand, in the National Comorbidity Survey the Composite International Diagnostic Interview was used to generate diagnoses according to the DSM-III-R criteria. A predominance of females was observed in lifetime prevalence rates of dysthymia (Table VI). The same study provided also twelve-month prevalence rates of dysthymia, these being 2.1% in males and 3.0% in females, with a female-to-male sex ratio of 1.4 (Kessler et al., 1994).

Intermittent depression, defined by the Schedule for Affective Disorders and Schizophrenia-Research Diagnostic Criteria, was investigated in a sample of first generation Jewish Israelis. At the
definite level of diagnostic confidence, six-month prevalence rates were 2.2% in males and 3.7% in females, with a female-to-male sex ratio of 1.7. The female-to-male sex ratio was 1.8, when intermittent depression was assessed according to both the definite and probable level of diagnostic confidence (Levav et al., 1993).

Finally, brief recurrent depression was investigated in a sample of young adults aged 23-24 years. Twelve-month prevalence rates were 3.9% in males and 4.9% in females, with a female-to-male sex ratio of 1.3. However, these rates were based on different thresholds for case-definition in males and females (3 criterion symptoms for males and 5 for females); using the same threshold in the two sexes, the female-to-male sex ratio was equal to 2.0 (Angst & Dobler-Mikola, 1985).

Table VI - Lifetime prevalence rates of dysthymia from general population studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample (N)</th>
<th>Age range (years)</th>
<th>Instruments</th>
<th>Diagnostic Criteria</th>
<th>Rates (%)</th>
<th>Female-to-Male Sex Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canino et al. (1987)</td>
<td>1,513</td>
<td>18 - 64</td>
<td>DIS</td>
<td>DSM-III</td>
<td>1.6:7.6:4.7</td>
<td>4.8:1</td>
</tr>
<tr>
<td>Puerto Rico, 1984</td>
<td></td>
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<tr>
<td>Bland et al. (1988b)</td>
<td>3,258</td>
<td>18 and over</td>
<td>DIS</td>
<td>DSM-III</td>
<td>2.2:5.2:3.7</td>
<td>2.4:1</td>
</tr>
<tr>
<td>Canada, 1983-86</td>
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<tr>
<td>Wells et al. (1989)</td>
<td>1,498</td>
<td>18 - 64</td>
<td>DIS</td>
<td>DSM-III</td>
<td>3.8:9.0:6.4</td>
<td>2.4:1</td>
</tr>
<tr>
<td>New Zealand, 1986</td>
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<tr>
<td>Lee et al. (1990a,b)</td>
<td>3,134</td>
<td>18 - 65</td>
<td>DIS</td>
<td>DSM-III</td>
<td>1.8*:3.0*:2.4*</td>
<td>1.7:1</td>
</tr>
<tr>
<td>Korea, n.r.</td>
<td>1,966</td>
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<tr>
<td>Robins &amp; Regier (1991)</td>
<td>18,571</td>
<td>18 and over</td>
<td>DIS</td>
<td>DSM-III</td>
<td>2.2:4.1:3.2</td>
<td>1.9:1</td>
</tr>
<tr>
<td>USA, 1980-83</td>
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<tr>
<td>Chen et al. (1993)</td>
<td>7,229</td>
<td>18 - 64</td>
<td>DIS</td>
<td>DSM-III</td>
<td>1.1:2.8:—</td>
<td>2.6:1</td>
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<tr>
<td>Hong Kong, 1984-86</td>
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<tr>
<td>Hwu et al. (1989)</td>
<td>11,004</td>
<td>18 and over</td>
<td>DIS</td>
<td>DSM-III</td>
<td>6.9*:11.4*:9.2*</td>
<td>1.7:1</td>
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<tr>
<td>Taiwan, 1982-85</td>
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<tr>
<td>Stefansson et al. (1991)</td>
<td>862</td>
<td>55 - 57</td>
<td>DIS</td>
<td>DSM-III</td>
<td>2.3:10.7:6.4</td>
<td>4.7:1</td>
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<tr>
<td>Iceland, 1987-88</td>
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<tr>
<td>Wittchen et al. (1992)</td>
<td>483</td>
<td>25 - 64</td>
<td>DIS</td>
<td>DSM-III</td>
<td>2.5:5.4:4.0</td>
<td>2.2:1</td>
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<tr>
<td>Germany, 1981</td>
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<tr>
<td>Kessler et al. (1994)</td>
<td>8,098</td>
<td>15 - 54</td>
<td>CIDI</td>
<td>DSM-III-R</td>
<td>4.8:8.0:6.4</td>
<td>1.7:1</td>
</tr>
<tr>
<td>USA, 1990-92</td>
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</tr>
</tbody>
</table>

a Urban area
b Rural area
c Metropolitan Taipei
d Small towns
e Rural villages
n.r. = not reported
PREVALENCE OF BIPOLAR DISORDER

Since prevalence of bipolar disorder is expected to be low in the general population, only lifetime prevalence rates by sex of respondents are reported in Table VII. Even in this case, gender differences should be interpreted with caution, due to the small number of individuals that satisfied lifetime criteria for bipolar disorder in most of the studies. The lifetime prevalence rates reported here included those subjects who ever met the criteria for bipolar I disorder during the entire lifespan prior to the examination.

Nine studies were based on the Diagnostic Interview Schedule and DSM-III criteria. The surveys carried out in Puerto Rico (Canino et al., 1987), Edmonton (Bland et al., 1988b), Christchurch (Wells et al., 1989), Korea (Lee et al., 1990a, b), the United States (Robins & Regier, 1991) and Hong Kong (Chen et al., 1993) were based on household probability samples of the general population. The Taiwan Psychiatric Epidemiology Project was carried out in three distinct populations in metropolitan, township and rural areas (Hwu et al., 1989). The study carried out in Iceland (Stefánsson et al., 1991) included half of the population born in Iceland in 1931 and living there in December 1986. Finally, the Münich Follow-up Study (Wittchen et al., 1992) was a seven-year prospective and retrospective follow-up investigation of a stratified random sample of the general population of former West Germany. The lifetime rates of bipolar disorder were generally lower than 1% (range between 0.2% and 1.6%); the female-to-male sex ratio ranged between 0.1 and 3.5.

Two studies were based on different research instruments and diagnostic criteria. Levav et al. (1993) assessed a sample of first generation Jewish Israelis, using the Schedule for Affective Disorders and Schizophrenia-Research Diagnostic Criteria. Rates of bipolar I disorder tended to be higher in females at both the definite and probable level of diagnostic confidence (Table VII). For bipolar II disorder, lifetime prevalence rates were 0.8% in males and 0.3% in females at the definite level of diagnostic confidence, with a female-to-male sex ratio of 0.4; the female-to-male sex ratio was 0.5, when bipolar II disorder was assessed according to both the definite and probable level of diagnostic confidence. On the other hand, in the National Comorbidity Survey the Composite International Diagnostic Interview was used to generate diagnoses according to the DSM-III-R criteria, with lifetime rates for bipolar disorder being similar in males and females (Kessler et al., 1994).
### Table VII - Lifetime prevalence rates of bipolar disorder from general population studies

<table>
<thead>
<tr>
<th>Author Country, time</th>
<th>Sample (N)</th>
<th>Age range (years)</th>
<th>Instruments Diagnostic Criteria</th>
<th>Males</th>
<th>Rates (%) Females</th>
<th>Total</th>
<th>Female-to-Male Sex Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canino et al. (1987)</td>
<td>1,513</td>
<td>18 - 64</td>
<td>DIS DSM-III</td>
<td>0.7</td>
<td>0.4</td>
<td>0.5</td>
<td>0.6 : 1</td>
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<tr>
<td>Puerto Rico, 1984</td>
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<td>Bland et al. (1988b)</td>
<td>3,258</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
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<td>0.4</td>
<td>0.6</td>
<td>0.6 : 1</td>
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<tr>
<td>Canada, 1983-86</td>
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<tr>
<td>Wells et al. (1989)</td>
<td>1,498</td>
<td>18 - 64</td>
<td>DIS DSM-III</td>
<td>0.5</td>
<td>0.9</td>
<td>0.7</td>
<td>1.8 : 1</td>
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<tr>
<td>New Zealand, 1986</td>
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<tr>
<td>Lee et al. (1990a,b)</td>
<td>3,134</td>
<td>18 - 65</td>
<td>DIS DSM-III</td>
<td>0.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.5 : 1</td>
</tr>
<tr>
<td>Korea, n.r.</td>
<td>1,966</td>
<td></td>
<td></td>
<td>0.8&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.1 : 1</td>
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<td>Chen et al. (1993)</td>
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<td>18 - 64</td>
<td>DIS DSM-III</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>1.0 : 1</td>
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<tr>
<td>Hong Kong, 1984-86</td>
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<tr>
<td>Hwu et al. (1989)</td>
<td>11,004</td>
<td>18 and over</td>
<td>DIS DSM-III</td>
<td>1.6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.0 : 1</td>
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<tr>
<td>Taiwan, 1982-85</td>
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<td></td>
<td>1.2&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.0&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.7&lt;sup&gt;d&lt;/sup&gt;</td>
<td>—</td>
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<tr>
<td>Stefansson et al. (1991)</td>
<td>862</td>
<td>55 - 57</td>
<td>DIS DSM-III</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>1.0 : 1</td>
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<td>Iceland, 1987-88</td>
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<tr>
<td>Wittchen et al. (1992)</td>
<td>483</td>
<td>25 - 64</td>
<td>DIS DSM-III</td>
<td>0.0</td>
<td>0.5</td>
<td>0.2</td>
<td>—</td>
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<tr>
<td>Germany, 1981</td>
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<tr>
<td>Levav et al. (1993)</td>
<td>2,741</td>
<td>24 - 33</td>
<td>SADS</td>
<td>0.5&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.8&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.7&lt;sup&gt;*&lt;/sup&gt;</td>
<td>1.6 : 1</td>
</tr>
<tr>
<td>Israel, 1982-88</td>
<td></td>
<td></td>
<td></td>
<td>0.2&lt;sup&gt;**&lt;/sup&gt;</td>
<td>0.7&lt;sup&gt;**&lt;/sup&gt;</td>
<td>0.5&lt;sup&gt;**&lt;/sup&gt;</td>
<td>3.5 : 1</td>
</tr>
<tr>
<td>Kessler et al. (1994)</td>
<td>8,098</td>
<td>15 - 54</td>
<td>CIDI DSM-III-R</td>
<td>1.6</td>
<td>1.7</td>
<td>1.6</td>
<td>1.1 : 1</td>
</tr>
<tr>
<td>USA, 1990-92</td>
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</tr>
</tbody>
</table>

* Either probable or definite level of diagnostic confidence
** Only definite level of diagnostic confidence

a Urban area
b Rural area
c Metropolitan Taipei
d Small towns
e Rural villages
n.r. = not reported
FACTORS THAT MAY INFLUENCE GENDER DIFFERENCES IN PREVALENCE RATES OF AFFECTIVE DISORDERS

A consistent finding from general population surveys of affective disorders concerns the higher rates of depressive disorders in females compared to males, whereas no or inconsistent gender differences were detected for bipolar disorder. However, it is still controversial whether gender differences in depressive disorders are real or an artifact. Four main issues should be considered that might affect gender differences in rates of depressive disorders: i) the definition of caseness and measurement procedures; ii) the recall bias; iii) the course of disorder and mortality rates; iv) the geographical mobility.

i) Definition of caseness and measurement procedures

A few studies examined the hypothesis that gender differences in rates of major depression depends on the criteria used to make the diagnosis. The diagnostic criteria for major depression set out by Spitzer et al. (1978) (Research Diagnostic Criteria), the American Psychiatric Association (DSM-III, DSM-III-R, DSM-IV) and the World Health Organization (ICD-10) are based on a number of criterion symptoms that are associated with depressed mood. Any general tendency for females to report more criterion symptoms than males may contribute to females being more likely to meet diagnostic criteria for major depression, if the same number of symptoms is required to make a diagnosis in both sexes.

In Zürich, Angst & Dobler-Mikola (1984) examined the 12-month prevalence rates of depressive episodes in a cohort of young adults aged 22-23 years. Among probands that reported episodes of depressed mood lasting two weeks or longer, females reported more symptoms compared to males, the median being five symptoms for females and three for males. Had the same number of depressive symptoms been required for both sexes to be assigned a diagnosis, then different rates of depressive disorder would be expected in males and females. Indeed, for the three months preceding examination, the female-to-male sex ratio of 0.6 for episodes of depressed mood turned to 1.9 and 1.8 when the Research Diagnostic Criteria and DSM-III criteria for major depression were applied, respectively. Moreover, males and females suffering from an episode of depressed mood of at least two-week duration gave similar ratings of subjective impairment and were equally impaired socially and occupationally. Thus, when the social impairment criteria were included in the diagnostic decision tree, an equal prevalence of depression was found in males and females. The Authors concluded that episodes of depression occurred at similar rates in males and females and any actual female preponderance resulted from excess reporting of depressive symptoms.
Different results were obtained by Fennig et al. (1994), who investigated the 12-month prevalence rates of DSM-III-R major depression in a relatively homogeneous population of managers and professionals from a large corporation. When the female-to-male sex ratio in rates of depression was examined by progressively increasing the number of symptoms required for a diagnosis of depressive episode, the female preponderance existed at each level, even though it became more pronounced as the number of symptoms increased. For each possible cut-off at five or more criterion symptoms (as required in DSM-III-R) the female-to-male sex ratio was near or above 2.0. The female preponderance persisted even if different cut-offs were used for assigning a diagnosis to males and females, that is five criterion symptoms for males and six for females. Finally, the pattern of association between depressive symptomatology and occupational impairment was very similar for males and females and the female-to-male sex ratio exceeded unity at all levels of impairment beyond the mildest. Thus, the pattern of higher female-to-male sex ratios was similar for the two systems of case identification (i.e., that based on symptoms and that based on impairment).

Similar findings were reported also by Kessler et al. (1993), using the data from the National Comorbidity Survey. About 46% of the males and 58% of the females reported the lifetime occurrence of at least one period of depressed mood or diminished interest in most of the normal activities lasting two weeks or longer. If endorsement of these stem questions was the only requirement for a diagnosis of depression, the female-to-male sex ratio was 1.3. The female-to-male sex ratio became progressively higher as the required number of criterion symptoms was increased: it was 1.7 when four or more criterion symptoms were required, as in the DSM-III-R criteria, and 2.5 when all the eight depressive symptoms included in DSM-III-R had to be present.

A true gender difference in lifetime rates of major depression rather than a general trend for females to report more criterion symptoms was suggested also by Young et al. (1990a) in a sample of first-degree relatives of probands who participated in the NIMH-Collaborative Study of the Psychobiology of Depression. Among those individuals who experienced depressed mood or loss of interest or pleasure of at least one week duration (criterion I of the Research Diagnostic Criteria) and impaired functioning or treatment-seeking (criterion II of the Research Diagnostic Criteria), similar proportions of males and females reported no, one and two criterion symptoms associated to depression. A gender difference in symptom count was found once three or more criterion symptoms were present (i.e., the cut-off used by the Research Diagnostic Criteria to make a lifetime diagnosis of past probable major depressive episode). The great bulk of the gender difference was based on only the depressed mood and impairment criteria, while using the criterion of three or more symptoms resulted in an increase in the female-to-male sex ratio of only 9%. Since for both males and females the discontinuity in the curve of symptom frequency occurred at the threshold level for a diagnosis of major depression
according to the Research Diagnostic Criteria, there was no support to the use of gender-specific threshold criteria.

In summary, although there is a tendency for females to report more criterion symptoms associated to depression compared to males, the findings available so far suggest that this does not seem to account entirely for gender differences in rates of major depression.

A related issue is whether males and females differ in the clinical manifestations of depression during a diagnosed depressive episode. Frank et al. (1988) reported on gender differences in a sample of 230 patients with recurrent depression. Females were more likely to report increased appetite and weight gain and less likely to report weight loss than their male counterparts; females also experienced more somatic anxiety, expressed anger and hypochondriasis. Similar results were found by Young et al. (1990b), who examined a sample of 498 probands seeking treatment for current nonpsychotic unipolar major depression according to the Research Diagnostic Criteria. Statistically significant differences were detected for two of the 41 clinical features considered, with increased appetite and weight gain occurring more frequently in females compared to males. Analysis of severity for those features that applied to all individuals showed no significant differences between males and females. Finally, Angst & Dobler-Mikola (1984) showed that females were more likely to report disturbance of appetite and sleep compared to males; in addition, reporting of symptoms by males tended to decrease and to be less reliable over a one-year period.

One approach to interpreting the results of these studies is to accept gender differences in clinical manifestations of depression as real; as an alternative interpretation, these findings might simply reflect sociocultural differences in the way males and females perceive their symptoms and respond to them (e.g., males might be engaged in more denial of symptoms than females, according to their socially desirable self-image). Whatever interpretation is endorsed, it might be expected that differences between males and females in experiencing or reporting depressive symptoms might lead to gender-specific response patterns depending on the individual items included in the rating scales for depression. Building on recent advances in structural equation models, Stommel et al. (1993) tested the degree to which the 20-item Center for Epidemiologic Studies Depression Scale (Radloff, 1977) was 'factorially invariant' across groups of male and female cancer patients. Two items were identified as producing biased responses according to sex of respondents: males, who otherwise had the same level of depressive symptoms as females, were less likely to have 'crying spells', but more likely to reduce their verbal communication ('talked less') compared to equally depressed females. When three additional items were excluded on the basis of other psychometric deficiencies, a subset of 15 items was left that captured almost all of the information of the original 20-item scale, but were free of any gender bias. Nevertheless, gender differences in mean levels of depressive symp-
tomatology, although significantly reduced, were not eliminated when the shortened version of the scale was used.

The psychometric properties of another well-known rating scale for depression (i.e., the Beck Depression Inventory - Beck et al., 1979) were compared in male and female psychiatric outpatients with affective disorders according to the DSM-III criteria. Only one of the 21 items differentiated males and females, with males reporting more severe self-dissatisfaction compared to females. Overall, the findings supported the comparability of the psychometric properties of the scale for both males and females and separate sex norms were not necessary for interpreting the scores reported on the scale (Steer et al., 1989).

**ii) Recall bias**

It has been suggested that the preponderance of females in rates of major depression might be the result of a gender difference in recalling past depressive episodes. The introduction of structured psychiatric interviews to generate standardized diagnostic decisions has raised the issues of test-retest reliability and inter-rater agreement as measures of the instrument error. A related paradigm is that of temporal stability, with agreement between assessments given at widely separated points in time (e.g., successive hospital admissions) reflecting 'true' lifetime clinical state and the validity of the underlying constructs (Rice et al., 1992).

Comparison of short-term and lifetime prevalence rates of major depression may provide indirect evidence of instability of results. In the NIMH-Epidemiologic Catchment Area Study the ratio of lifetime to six-month prevalence rates of major depression was 2.0, indicating that half of the subjects reporting a lifetime episode of major depression had it in the six months preceding the examination (Weissman et al., 1988). Similar findings were reported by other general population studies using the Diagnostic Interview Schedule and DSM-III criteria: the ratios of lifetime to six-month prevalence rates of major depression were 1.5 in Puerto Rico (Canino et al., 1987), 2.3 in Iceland (Stefánsson et al., 1991; 1994), 2.4 in Christchurch (Wells et al., 1989; Oakley-Browne et al., 1989), 2.7 in Edmonton (Bland et al., 1988 a, b) and 3.0 in München (Wittchen et al., 1992). Although it cannot be excluded that subjects reporting major depression have depressive episodes that are long and/or highly recurrent, these findings suggest that remote episodes might be forgotten, resulting in an under-estimate of lifetime rates of depression. Indeed, Parker (1987) raised doubts about the validity of the lifetime prevalence estimates generated in the reports of the Epidemiologic Catchment Area Study and identified three reasons to suspect their accuracy: the ratio of lifetime and six-month prevalence data, the discordance with previous estimates of lifetime morbidity, and the curvilinear association of lifetime prevalence estimates with increasing age.