

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, there 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 becomes 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 nor 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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