Sex Differences in the Prevalence and Detection of Depressive and Anxiety Disorders in General Health Care Settings

Report From the World Health Organization Collaborative Study on Psychological Problems in General Health Care

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Background: Understanding the relevance of biological and social factors to sex differences in the prevalence and detection of depressive and anxiety disorders has been impeded by the lack of standardized research methods across cultures.

Method: Prevalence rates of depressive and anxiety disorders were assessed using a 2-stage design from 26,969 patients attending for primary care in 15 centers from 4 continents. Logistic regression analysis was used to examine sex differences in prevalence and detection across centers.

Results: Odds ratios for women compared with men of current depression (1.60; 95% confidence interval [CI], 1.37-1.86) and agoraphobia or panic (1.63; 95% CI, 1.18-2.20) were consistent across centers. The odds ratio for generalized anxiety varied among centers: 3 groups of centers were identified with odds ratios of 0.46 (95% CI, 0.27-0.78), 1.34 (95% CI, 1.08-1.66), and 3.09 (95% CI, 1.60-5.89). There was no sex difference in the detection of depressive and anxiety disorders by physicians across centers.

Conclusions: The absence of a sex-by-center effect for current depression and agoraphobia or panic disorder is consistent with biological and psychosocial factors, either interacting or working alone, that have a similar final effect across cultures. It does not support the idea that sex differences in prevalence are caused by local psychosocial factors that vary from country to country. The variation in the odds ratio for generalized anxiety disorder offers some support to the idea that there are local differences between the centers contributing to the sex difference in rates. Patients’ sex does not appear to affect the likelihood of current depression and anxiety being detected by primary care physicians.

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A female preponderance of depressive disorders has been a consistent observation in community care surveys. The female-male ratio for current depression calculated from reported rates in the community often falls between 1.3 and 2.8. The female-male ratio for anxiety disorders calculated from published community rates varies from 0.7 in Canberra, Australia, to 4.5 in London, England, and 4.8 in Santander, Spain. Studies in primary care settings have seldom reported prevalence by sex for individual disorders, but when this has been done, prevalence rates were higher in women than in men for all categories of depressive disorder, whereas rates of anxiety were lower in women than in men. Previous studies have reported on the detection by primary care physicians of depressive and anxiety disorders in men and women. It is difficult to interpret variations between prevalence and detection rates from different studies because of differences in survey methods, particularly the methods of sample selection and diagnosis. Nevertheless, the investigation of cross-cultural variations in the sex ratio of rates of disorders can contribute to our understanding of the causative factors underlying the observed difference in rates. Biological factors, experience, and circumstances are continuously interacting and influencing each other in emotional development and expression and in the cause of mental disorders. Previous research has produced evidence that sex differences in the rates of mental disorders are related to the different social roles of men and women. If such factors are important and vary among cultures, they are likely to be reflected in sex ratios that vary among cultures.
METHODS

The World Health Organization Psychological Problems in General Health Care study has investigated the form, frequency, management, and outcome of common psychological disorders in primary care patients. Participating centers are in Ankara, Turkey; Athens, Greece; Bangalore, India; Berlin, Germany; Groningen, the Netherlands; Ibadan, Nigeria; Mainz, Germany; Manchester, England; Nagasaki, Japan; Paris, France; Rio de Janeiro, Brazil; Santiago, Chile; Seattle, Wash; Shanghai, China; and Verona, Italy. The choice of centers was made taking into account the need to select from a variety of countries, the availability of previous community and primary care surveys for comparison, and the capability of centers to carry out research using standardized instruments and epidemiological methods. The general health care clinics were selected to be prototypically representative of primary health care services in their country, and, wherever possible, atypical or university-based clinics were avoided. The participating clinics varied in type, organization, and the sociodemography, presenting symptoms, and physical and mental disorders of their patients (Table 1). Full descriptions of each of the centers and of the study methods have been published elsewhere.27

SAMPLING PROCEDURE

The study used a 2-stage sampling procedure: a first-stage screening followed by a second-stage standardized in-person interview of a selected sample. In the first stage, consecutive patients, between the ages of 18 and 65 years, who were attending primary care clinics were administered the 12-item General Health Questionnaire (GHQ)28 by a research worker. Respondents completed this written screening questionnaire, or, if they were not able to read or write, the questionnaire was administered verbally following a standard protocol. For the second stage, a stratified random sample was selected for interview. Samples were drawn from 3 GHQ strata: 100% of patients with a high GHQ score, a random sample of 35% of medium scorers, and a random sample of 10% of low scorers. Based on the GHQ distribution for each sex at each center, high scorers were defined as the highest 20% at the center, medium scorers were the next 20%, and the remaining 60% were classified as low GHQ scorers.

Second-Stage Assessment

For the second-stage assessment, we used the primary care version of the Composite International Diagnostic Interview (CIDI).29 The CIDI was selected because there are explicit diagnostic algorithms for International Statistical Classification of Diseases, 10th Revision (ICD-10),30 and DSM-III-R31 diagnoses; it has high interrater reliability; and it has been translated, backtranslated, and tested in the different languages relevant to the centers involved in the study. Several other instruments were also included in the second-stage interview to collect information on the main symptoms, pathways to care, physical and psychological comorbidity, social disability, and self-rated health status.32 The assessments were carried out by interviewers who received uniform training and met a high standard of interrater reliability.37

For each patient selected, the primary care physician who treated the patient completed a brief Physician’s Encounter Form to indicate his or her assessment of the patient’s current physical and psychological status and the management of the case. The primary care physician was asked to rate each patient’s mental health status on a 5-point scale, according to whether the physician thought the patient was completely normal (1 point); had some psychological symptoms but was not mentally ill (2 points);

RESULTS

In total, from the 15 centers, 26,969 primary care patients were eligible for screening, of whom 25,916 (96.1%) completed the 12-item GHQ (Table 2). From all centers, 62% of those screened were women, ranging from 47% in Paris to 73% in Ibadan. Second-stage interviews were completed on 5438 patients, representing 64.9% of those eligible. There was some variation between centers in the response rate for the second-stage interview. The method of weighting study data, however, was adjusted to take account of nonresponse according to sex and GHQ score stratum for each center.

CURRENT DEPRESSIVE EPISODE

The average prevalence for an ICD-10 current depressive episode among men was 7.1% (95% confidence interval [CI], 6.0%-8.3%) compared with 12.5% (95% CI, 11.5%-13.7%) among women (Table 3). Most centers had higher rates in women, and this reached significance at the 5% level in Bangalore, Paris, Rio de Janeiro, and Santiago.

The results of the LR analyses, with the current depressive episode as the dependent variable for all centers combined, are shown in Table 4. The sex-by-center interaction was not significant (LR, \( \chi^2_{14} = 20.53; P = .11 \)). Therefore, the odds of depression for women com-

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or had a case of mild (3 points), moderate (4 points), or severe (5 points) psychological disorder. The physicians made their ratings using all the information normally available to them at the index consultation, but they were not aware of the results of the screening test.

Case Definition and Diagnostic Classification

Responses to the CIDI were used to make ICD-10 diagnoses for the current depressive episode, generalized anxiety disorder (GAD), and agoraphobia or panic disorder using a computer algorithm based on the ICD-10 Diagnostic Criteria for Research. Prevalence rates were calculated using weights that reflected the probabilities of selection into the sample according to sex and GHQ score, adjusted for nonresponse. The weighting procedure took account of the differences in cutoff points and response rates across centers. Therefore, the reported rates are unbiased estimates of the prevalence of each disorder among all consecutive patients attending at the respective primary care sites.

STATISTICAL ANALYSIS

For each center, prevalence rates for men and women were compared using the Fisher exact test. To test whether sex differences were consistent across centers, logistic regression (LR) analysis was used with the disorder of interest as the dependent variable, and sex, center, and sex-by-center interaction entered as independent variables. A significant sex-by-center interaction term indicates that the centers differ in the sex ratio of the disorder. Post hoc comparisons of coefficients were used to show any centers that were outliers. The effects of possible confounders were tested one by one. Results are presented in the form of odds ratios (ORs) for women compared with men when all other variables in the model are held constant. Model 1 contains only sex and center as independent variables, so the OR presented represents the increase in the odds of the disorder for women compared with men, adjusting for center. Model 2 includes sex, center, and GHQ stratum. All other models presented in the tables include the independent variables sex, center, GHQ stratum, and the confounding variable of interest. Confounding variables are included in the model singly because small numbers in individual cells lead to unstable estimates if all are included simultaneously. Data were unweighted for all LR analyses.

The following possible confounding variables, which vary considerably between centers and are associated with sex, were considered: comorbid disorders, GHQ stratum, age (coded 18-24, 25-44, and 45-65 years), education (<8, 9-13, and >13 years), marital status (never married; currently married; or widowed, separated, or divorced), employment status (employed, unemployed, or keeping house), and number of children (0 or 1; and ≥2). The samples were representative of the primary care services investigated but may not have been representative of the communities from which they came. Therefore, apparent sex differences in rates among patients attending primary care clinics could be accounted for by variations in sex differences in care-seeking behavior. To examine this possibility, the time since the last appointment was included in the LR analyses as a proxy measure of care seeking.

Logistic regression models were also used to investigate whether primary care physicians differ across centers in their detection rates by sex of the patients. The dependent variable was the presence of a diagnosis of depressive or anxiety disorder according to ICD-10 criteria, as determined by the primary care physician, and independent variables were the CIDI diagnosis, sex, center, and their interaction terms. The possible effects of confounding variables were also investigated. The pattern of significant interaction terms determines how detection rates vary by sex and disorder across centers. Unless otherwise stated, α levels of .05 have been used.

Pared with men could be estimated across all centers simultaneously: this was found to be 1.60 (95% CI, 1.37-1.86). When adjusted for other possible confounding variables, the ORs varied only slightly, as shown in Table 4. The interaction terms of each possible confounder with sex was tested for each model and found to be nonsignificant for all, except parity. The odds of depression among women with 2 or more children was slightly higher than for women with no children or 1 child (OR = 1.57 as compared with 1.41; P = .02). The size of the difference, although statistically significant, is slight. Although most potential confounders were significantly associated with a major depressive episode, the association was independent of the sex of the patient.

GENERALIZED ANXIETY DISORDER

The average rate of GAD for men is 5.7% (95% CI, 4.7%-6.8%) and for women is 9.2% (95% CI, 8.3%-10.3%), but there appears to be considerable variation in the rates across centers (Table 3). In most centers, the rate is higher among women than among men, and there was a significantly higher prevalence of GAD among women in Berlin, Groningen, and Rio de Janeiro. In 3 centers—Ibadan, Nagasaki, and Seattle—there is a tendency for women to have lower rates than men. In some centers, relative to the average, there are particularly high rates in women (eg, Rio de Janeiro and Santiago), whereas in other centers, there are particularly low rates in men (eg, Groningen and Verona).

In the LR analysis with GAD as the dependent variable, the sex-by-center interaction was significant (LR, χ² = 27.4; P = .02). Therefore, the odds of GAD for women compared with men could not be estimated across all centers. This interaction remained significant after adjustments for the GHQ stratum, comorbid current depressive episode, and age (LR, χ² = 23.7; P = .049). A post hoc examination of the interaction terms showed that the centers could be split into 3 different groups. Group 1, comprising Groningen and Verona, had much higher odds of GAD in women than in men (3.09; 95% CI, 1.60-5.89). Group 2 contained most of the centers: Ankara, Athens, Bangalore, Berlin, Mainz, Manchester, Paris, Rio de Janeiro, Santiago, and Shanghai. Women were more likely than men to be diagnosed as having GAD, but the OR (1.34; 95% CI, 1.08-1.66) was smaller than for the
centers in group 1. Group 3 consisted of the centers in Ibadan, Seattle, and Nagasaki, where women were significantly less likely than men to be diagnosed as having GAD (OR, 0.46; 95% CI, 0.27-0.78).

When adjusted for other possible confounding variables, the ORs varied only slightly (Table 5). The interaction terms of each possible confounder with sex were tested and found to be nonsignificant except for marital status, which presented a complex picture. To interpret the coefficients, separate analyses were done for the group of patients who were currently married and a second group of patients who were single, widowed, separated, or divorced (“not currently married”). Odds ratios for women being diagnosed as having GAD compared with men were obtained. For the group 1 centers, the OR of GAD for married women compared with married men is 2.4 (95%
CI, 1.1-5.3), whereas among those not currently married, the OR for women compared with men is higher at 5.2 (95% CI, 1.5-18.8). For the group 2 centers, the OR of GAD for women compared with men was significant only for those who were currently married (OR, 1.65; 95% CI, 1.22-2.24). Among those not currently married, the OR for women compared with men was 0.87 (95% CI, 0.62-1.21). Finally, for the group 3 centers, there was no sex-by-marital status interaction and no differences in the GAD according to marital status.

AGORAPHOBIA AND PANIC DISORDER

The rates for agoraphobia and panic disorder were lower than those for the other diagnoses, and these 2 disorders were combined and analyzed together. The overall average prevalence of agoraphobia or panic disorder was 1.5% (95% CI, 1.0%-2.1%) in men and 2.8% (95% CI, 2.2%-3.4%) in women (Table 3). In only 1 center (Paris) were the rates significantly higher in women. Elsewhere the comparison of rates within each center did not reveal any significant differences in the rates in men compared with women, although the small number involved limits the power of these comparisons.

The results of the LR analyses, with agoraphobia or panic disorder (or both) as the dependent variable, are shown in Table 6. The sex-by-center interaction was not significant (LR, \( \chi^2_{14} = 14.54; P = .41 \)), and the odds of agoraphobia and panic disorder for women compared with men could be estimated across all centers simultaneously. This was found to be 1.63 (95% CI, 1.18-2.20). When adjusted for other possible confounding variables, the OR varied only slightly. The interaction terms of each possible confounder with sex was tested and found to be nonsignificant.

DETECTION OF CIDI CASES BY PRIMARY CARE PHYSICIANS

When each center was analyzed separately, in none were there significant differences in the detection rates of ICD-10 depressive and anxiety disorders for male patients compared with female patients. A series of LR analyses were made with detection by the primary care physician as the dependent variable and sex, center, CIDI diagnosis, and GHQ stratum and their interaction terms as independent variables. Because there were significant interaction terms between the diagnostic variables, sex and center, the analysis was conducted for 2 groups separately: 1 group of all subjects given a CIDI diagnosis of 1 or more of the depressive and anxiety disorders and a second group of those who received none of these diagnoses. For these separate LR analyses, interaction terms involving a center were not significant, and therefore an analysis for all centers combined could be made. Among subjects with a CIDI diagnosis, there is no difference between men and women in the odds of being given a psychological diagnosis by the primary care physician, controlling for center and GHQ stratum (OR for detection for women compared with men, 0.94; 95% CI, 0.79-1.21). Among those subjects who did not re-
ceive a CIDI diagnosis, however, the odds of a woman being reported by the physician as having a psychological diagnosis are slightly higher than that for a man (OR, 1.20; 95% CI, 1.01-1.43). When the estimates of the odds ratios are adjusted for confounding variables (age, education, marital status, parity, employment, and frequency of consultation), the individual ORs vary only slightly. Confounding variables were related to the odds of detection, but no interaction terms between these and sex were found. That is, the detection of a case of a psychological disorder associated with sex does not alter according to whether confounding variables were present.

The odds of a current depressive episode for women compared with men across all centers were estimated to be 1.60, and for agoraphobia and panic disorder, the OR was 1.63. The absence of a sex-by-center effect suggests that the causes of a higher rate in women for these disorders are having a similar resultant effect in all centers. This does not support the idea that the sex difference in rates is caused by local psychosocial effects that vary from one society to another. It is compatible with biological or psychosocial factors, either interacting or working alone, that have a similar final effect across cultures.

In contrast, the odds for men and women of GAD vary between centers. In some centers, Groningen and Verona (group 1), the odds of having generalized anxiety are 3 times higher for women than for men. In most centers (group 2), there is a modest OR of 1.3, and in a few centers (group 3), the odds for women are half those for men. These findings offer support to the idea that there are differences between the centers that contribute to the sex difference in rates of GAD, such as differences in the social roles and experiences of women and men. Our findings also suggest different effects of marital status for men and women when these 3 groups of centers are analyzed separately. An important reason for carrying out this post hoc separation of the centers into 3 groups is to try to present the results in a manner that allows a nonstatistical evaluation. The grouping of centers, however, does not fall into a pattern that is culturally recognizable, and the health care centers do not have characteristics that

Table 3. Prevalence by Sex and Sex Ratios of Composite International Diagnostic Interview–Derived ICD-10 Depressive and Anxiety Disorders for Each Center

<table>
<thead>
<tr>
<th>Center</th>
<th>Current Depressive Episode</th>
<th>Generalized</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. †</td>
<td>Women</td>
</tr>
<tr>
<td>Ankara, Turkey</td>
<td>105</td>
<td>12.5</td>
</tr>
<tr>
<td>Athens, Greece</td>
<td>34</td>
<td>6.4</td>
</tr>
<tr>
<td>Bangalore, India</td>
<td>72</td>
<td>13.3</td>
</tr>
<tr>
<td>Berlin, Germany</td>
<td>62</td>
<td>7.7</td>
</tr>
<tr>
<td>Groningen, the Netherlands</td>
<td>121</td>
<td>17.9</td>
</tr>
<tr>
<td>Ibadan, Nigeria</td>
<td>23</td>
<td>3.8</td>
</tr>
<tr>
<td>Mainz, Germany</td>
<td>62</td>
<td>12.3</td>
</tr>
<tr>
<td>Manchester, England</td>
<td>154</td>
<td>18.3</td>
</tr>
<tr>
<td>Nagasaki, Japan</td>
<td>25</td>
<td>2.8</td>
</tr>
<tr>
<td>Paris, France</td>
<td>132</td>
<td>18.7</td>
</tr>
<tr>
<td>Rio de Janeiro, Brazil</td>
<td>119</td>
<td>19.6</td>
</tr>
<tr>
<td>Santiago, Chile</td>
<td>117</td>
<td>36.8</td>
</tr>
<tr>
<td>Seattle, Wash</td>
<td>61</td>
<td>6.5</td>
</tr>
<tr>
<td>Shanghai, China</td>
<td>53</td>
<td>4.4</td>
</tr>
<tr>
<td>Verona, Italy</td>
<td>34</td>
<td>5.5</td>
</tr>
<tr>
<td>Totals</td>
<td>1174</td>
<td>12.5</td>
</tr>
</tbody>
</table>

*ICD-10 indicates International Statistical Classification of Diseases, 10th Revision; question mark, unknown.
† Number of patients with the disorder interviewed.
‡ Estimated percentage of consecutive patients attending the center who have the disorder.
§ P < .01.
|| P < .05.

Table 4. Results of the Logistic Regression Analyses With the Current Depressive Episode as the Dependent Variable for All Centers

<table>
<thead>
<tr>
<th>Model†</th>
<th>Odds Ratio (95% CI) of Current Depressive Episode for Women Compared With Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex + center</td>
<td>1.60 (1.37-1.86)</td>
</tr>
<tr>
<td>Model 1 + GHQ stratum</td>
<td>1.52 (1.29-1.75)</td>
</tr>
<tr>
<td>Model 2 + GAD</td>
<td>1.52 (1.29-1.52)</td>
</tr>
<tr>
<td>Model 2 + age</td>
<td>1.52 (1.30-1.78)</td>
</tr>
<tr>
<td>Model 2 + marital status‡</td>
<td>1.48 (1.26-1.74)</td>
</tr>
<tr>
<td>Model 2 + parity‡</td>
<td>§</td>
</tr>
<tr>
<td>Model 2 + employment‡</td>
<td>1.51 (1.28-1.79)</td>
</tr>
<tr>
<td>Model 2 + education</td>
<td>1.49 (1.28-1.75)</td>
</tr>
<tr>
<td>Model 2 + time since last visit</td>
<td>1.51 (1.28-1.76)</td>
</tr>
</tbody>
</table>

* CI indicates confidence interval; GHQ, General Health Questionnaire; and GAD, generalized anxiety disorder.
† Variables included in the model as independent terms. Interaction terms of each confounding variable with sex were tested and found to be nonsignificant, except for parity by sex.
‡ Main effect nonsignificant.
§ The odds ratio (95% CI) for women with 0 to 1 child compared with men is 1.41 (1.19-1.67) and for women with <2 children compared with men is 1.57 (1.29-1.91).
fall into these 3 groups. Although the status of GAD as an independent diagnosis has been questioned,34-36 there is no reason to suppose that in the different centers this disorder has been assessed less consistently than the other disorders.

There are no intercenter differences in the odds of detection for women compared with men. In fact, the detection of ICD-10 cases of depressive and anxiety disorders is similar for men and women in every center. Therefore, sex does not appear to affect the likelihood of depressive and anxiety disorders being detected by primary care physicians.

The Psychological Problems in General Health Care study provides an excellent opportunity to look for differences across centers because the same method has been used in 15 different centers around the world. The analysis is complex, however, and it is important not to read too much into the data. This study recruited from primary care practices, which may not reflect the situation in the community. Because the time since the last ap-
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Table 6. Results of the Logistic Regression Analyses With Agoraphobia or Panic Disorder as the Dependent Variable for All Centers*

<table>
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<tr>
<th>Model</th>
<th>Odds Ratio (95% CI) of Current Agoraphobia or Panic Disorder for Women Compared With Men</th>
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<tbody>
<tr>
<td>Sex + center</td>
<td>1.63 (1.18-2.20)</td>
</tr>
<tr>
<td>Model 1 + GHQ stratum</td>
<td>1.53 (1.12-2.12)</td>
</tr>
<tr>
<td>Model 2 + depressive episode</td>
<td>1.41 (1.04-2.04)</td>
</tr>
<tr>
<td>Model 2 + age</td>
<td>1.55 (1.12-2.15)</td>
</tr>
<tr>
<td>Model 2 + marital status</td>
<td>1.54 (1.09-2.10)</td>
</tr>
<tr>
<td>Model 2 + parity</td>
<td>1.54 (1.10-2.15)</td>
</tr>
<tr>
<td>Model 2 + employment</td>
<td>1.52 (1.07-2.16)</td>
</tr>
<tr>
<td>Model 2 + education</td>
<td>1.54 (1.11-2.13)</td>
</tr>
<tr>
<td>Model 2 + time since last visit</td>
<td>1.55 (1.12-2.15)</td>
</tr>
</tbody>
</table>

*CI indicates confidence interval; GHQ, General Health Questionnaire.
†Variables included in the model as independent terms. Interaction terms of each confounding variable with gender were tested and found to be nonsignificant.

References


