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## AN INTERNATIONAL STUDY OF THE RELATION BETWEEN SOMATIC SYMPTOMS AND DEPRESSION

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### ABSTRACT

**Background** Patients with depression, particularly those seen by primary care physicians, may report somatic symptoms, such as headache, constipation, weakness, or back pain. Some previous studies have suggested that patients in non-Western countries are more likely to report somatic symptoms than are patients in Western countries.

**Methods** We used data from the World Health Organization's study of psychological problems in general health care to examine the relation between somatic symptoms and depression. The study, conducted in 1991 and 1992, screened 25,916 patients at 15 primary care centers in 14 countries on 5 continents. A total of 5447 of the patients underwent a structured assessment of depressive and somatoform disorders.

**Results** A total of 1146 patients (weighted prevalence, 10.1 percent) met the criteria for major depression. The range of patients with depression who reported only somatic symptoms was 45 to 95 percent (overall prevalence, 69 percent;  $P=0.002$  for the comparison among centers). A somatic presentation was more common at centers where patients lacked an ongoing relationship with a primary care physician than at centers where most patients had a personal physician (odds ratio, 1.8; 95 percent confidence interval, 1.2 to 2.7). Half the depressed patients reported multiple unexplained somatic symptoms, and 11 percent denied psychological symptoms of depression on direct questioning. Neither of these proportions varied significantly among the centers. Although the overall prevalence of depressive symptoms varied markedly among the centers, the frequencies of psychological and physical symptoms were similar.

**Conclusions** Somatic symptoms of depression are common in many countries, but their frequency varies depending on how somatization is defined. There is substantial variation in how frequently patients with depression present with strictly somatic symptoms. In part, this variation may reflect characteristics of physicians and health care systems, as well as cultural differences among patients. (N Engl J Med 1999;341:1329-35.)

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**S**OMATIZATION is a frequently cited feature of depression in patients seen by primary care physicians.<sup>1-3</sup> Some studies suggest that patients in non-Western cultures or developing countries report somatic symptoms and deny psychological symptoms more frequently than patients in Western or developed countries.<sup>4-7</sup> One conclusion drawn from these data is that patients from non-Western cultures and those of lower socioeconomic status are less willing or less able to express emotional distress.<sup>8-11</sup> Epidemiologic data, however, have not shown cross-national differences in the somatization of depression. Community surveys with the use of standardized interviews have shown a similar balance between psychological and somatic symptoms in non-Western and Western countries.<sup>12</sup> According to data from clinical studies in which structured interviews were used, the reporting of somatic symptoms by depressed patients is widespread.<sup>7,13,14</sup>

As Kirmayer and Robbins<sup>15,16</sup> and Kellner<sup>17</sup> have noted, the term "somatization" refers to a variety of phenomena. We identified three different definitions of somatization used in earlier investigations. The first emphasizes presentation with somatic symptoms. Goldberg and Bridges<sup>18,19</sup> point out that many patients with psychiatric disorders seek care for somatic symptoms. According to this definition, patients with somatization are those who have psychiatric disorders but who present with somatic symptoms. The

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The investigators who participated in the study are listed in the Appendix.

second definition emphasizes the association between depression and medically unexplained somatic symptoms.<sup>20-23</sup> Barsky<sup>24</sup> describes the influence of psychological distress on the perception or reporting of somatic symptoms as “somatosensory amplification.” According to this view, patients with somatization are those who have psychological disorders but who report multiple unexplained somatic symptoms. The third definition emphasizes the denial of psychological distress and the substitution of somatic symptoms. From this perspective, somatization is a psychological defense against the awareness or expression of psychological distress. Nemiah<sup>25</sup> and Lesser<sup>26</sup> view somatization as related to alexithymia (the inability to express feelings). Kleinman<sup>27,28</sup> has described somatic symptoms as an alternative “idiom of distress” that is prevalent in cultures where psychiatric disorders carry great stigma.

We used data from the World Health Organization (WHO) collaborative study of psychological problems in general health care to examine the somatization of depression in primary care settings in countries representing a range of cultures, levels of economic development, and types of health care delivery. We used standardized measures in 14 countries on 5 continents. This allowed an assessment of cross-national differences that was more comprehensive than previous assessments.

## METHODS

### Study Design

The WHO collaborative study examined the epidemiology of common psychological disorders among patients visiting primary care clinics in Ankara, Turkey; Athens, Greece; Bangalore, India; Berlin, Germany; Groningen, the Netherlands; Ibadan, Nigeria; Mainz, Germany; Manchester, United Kingdom; Nagasaki, Japan; Paris, France; Rio de Janeiro, Brazil; Santiago, Chile; Seattle; Shanghai, China; and Verona, Italy. Centers were recruited on the basis of geographic diversity, previous success in collaborative research, and access to primary care facilities considered to be representative of local facilities. The study protocol was approved by local ethics or institutional review boards at all centers. Written informed consent was obtained from all patients. The study methods are described in detail elsewhere<sup>29,30</sup> and are summarized here.

During the period from May 1991 to April 1992, each center screened a consecutive or random sample of patients between the ages of 18 and 64 years who were seeking care at primary care facilities. Before the visit, patients were asked to complete the 12-item General Health Questionnaire,<sup>31</sup> a self-reported measure of general psychological distress. A total of 25,916 patients completed the questionnaire. The overall response rate was 96 percent (range, 91 to 100). Patients were selected for the second-stage diagnostic assessment on the basis of score thresholds that varied according to the center (100 percent of patients with scores on the General Health Questionnaire that exceeded the 80th percentile for the particular center were selected, as well as 35 percent of patients scoring between the 60th and 80th percentiles and 10 percent of patients scoring below the 60th percentile).<sup>32</sup> Among the 8785 patients who met the criteria to be selected for the second-stage interview, the response rate was 62 percent (range, 43 to 99). Respondents and nonrespondents did not differ significantly with respect to age, sex, or score on the General Health Questionnaire.

**TABLE 1.** CLASSIFICATIONS OF THE STUDY CENTERS.\*

| Type A center                    | Type B center                   |
|----------------------------------|---------------------------------|
| Athens, Greece†                  | Ankara, Turkey                  |
| Berlin, Germany                  | Athens, Greece†                 |
| Groningen, the Netherlands       | Bangalore, India                |
| Mainz, Germany                   | Ibadan, Nigeria                 |
| Manchester, United Kingdom       | Nagasaki, Japan                 |
| Paris, France                    | Rio de Janeiro, Brazil          |
| Santiago, Chile                  | Shanghai, China                 |
| Seattle                          |                                 |
| Verona, Italy                    |                                 |
| Higher level of development      | Lower level of development      |
| Berlin, Germany                  | Ankara, Turkey                  |
| Groningen, the Netherlands       | Athens, Greece                  |
| Mainz, Germany                   | Bangalore, India                |
| Manchester, United Kingdom       | Ibadan, Nigeria                 |
| Nagasaki, Japan                  | Rio de Janeiro, Brazil          |
| Paris, France                    | Santiago, Chile                 |
| Seattle                          | Shanghai, China                 |
| Verona, Italy                    |                                 |
| Western Europe and North America | Africa, Asia, and South America |
| Athens, Greece                   | Ankara, Turkey                  |
| Berlin, Germany                  | Bangalore, India                |
| Groningen, the Netherlands       | Ibadan, Nigeria                 |
| Mainz, Germany                   | Nagasaki, Japan                 |
| Manchester, United Kingdom       | Rio de Janeiro, Brazil          |
| Paris, France                    | Santiago, Chile                 |
| Seattle                          | Shanghai, China                 |
| Verona, Italy                    |                                 |

\*Type A centers were characterized by ongoing patient–physician relationships, scheduled appointments, detailed medical records, and an emphasis on the privacy of the visit. Type B centers were characterized by unscheduled appointments and patient–physician relationships that were not ongoing. The level of economic development was based on the United Nations Human Development Index for 1992.<sup>35</sup>

†One of two clinics in Athens was classified as type A, and the other as type B.

In the second-stage evaluation (involving 5447 patients), we used a primary care version of the Composite International Diagnostic Interview,<sup>33</sup> a fully structured diagnostic interview developed by WHO for use in cross-national psychiatric studies. Depression was assessed according to the nine criteria listed in the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV),<sup>1</sup> for the diagnosis of a major depressive episode: depressed mood, loss of interest in activities, change in weight or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue, feelings of worthlessness or inappropriate guilt, impaired concentration or memory, and suicidal ideation. Somatization was assessed according to the symptoms listed in DSM-IV<sup>1</sup> or the *International Classification of Diseases, 10th Revision* (ICD-10),<sup>2</sup> as diagnostic criteria for somatoform disorders. The interviewer first determined whether each symptom had ever occurred (e.g., “Have you ever had a lot of trouble with back pain?”). For each positive response, the interviewer asked a structured sequence of questions to determine whether the symptom was clinically important and to obtain specific information about its cause (e.g., questions about whether diagnostic testing had been done and whether a diagnosis had been made). A physician reviewer at each center classified each symptom as medically explained or unexplained. Standard diagnostic-interview questions about lifetime history were supplemented with questions about current symptoms. Additional questions concerned presenting symptoms or reasons for seeking care (up to three were recorded).

The severity of medical illness was assessed with the use of both a checklist of 20 chronic medical conditions, which the pa-

**TABLE 2.** PREVALENCE OF SOMATIZATION, ACCORDING TO VARIOUS DEFINITIONS, AMONG PATIENTS WITH MAJOR DEPRESSION.

| LOCATION OF CENTER         | MAJOR DEPRESSION    |                         | DEFINITION OF SOMATIZATION*   |                              |                                  |     |     |
|----------------------------|---------------------|-------------------------|-------------------------------|------------------------------|----------------------------------|-----|-----|
|                            | WEIGHTED PREVALENCE | UNWEIGHTED NO. OF CASES | SOMATIC PRESENTATION          | UNEXPLAINED SOMATIC SYMPTOMS | DENIAL OF PSYCHOLOGICAL SYMPTOMS | ANY | ALL |
|                            | %                   |                         | % of patients with depression |                              |                                  |     |     |
| Ankara, Turkey             | 10.8                | 94                      | 95                            | 51                           | 5                                | 94  | 2   |
| Athens, Greece             | 7.1                 | 38                      | 91                            | 36                           | 26                               | 88  | 10  |
| Bangalore, India           | 8.5                 | 70                      | 87                            | 62                           | 4                                | 94  | 1   |
| Berlin, Germany            | 5.3                 | 54                      | 74                            | 40                           | 26                               | 88  | 11  |
| Groningen, the Netherlands | 14.4                | 108                     | 67                            | 61                           | 14                               | 86  | 6   |
| Ibadan, Nigeria            | 4.1                 | 25                      | 88                            | 42                           | 17                               | 90  | 4   |
| Mainz, Germany             | 10.0                | 55                      | 85                            | 30                           | 15                               | 93  | 4   |
| Manchester, United Kingdom | 17.1                | 159                     | 60                            | 40                           | 14                               | 73  | 2   |
| Nagasaki, Japan            | 1.5                 | 16                      | 77                            | 50                           | 20                               | 77  | 13  |
| Paris, France              | 13.6                | 128                     | 45                            | 47                           | 12                               | 77  | 2   |
| Rio de Janeiro, Brazil     | 18.3                | 151                     | 69                            | 60                           | 2                                | 89  | 0   |
| Santiago, Chile            | 27.3                | 117                     | 68                            | 59                           | 5                                | 88  | 3   |
| Seattle                    | 6.4                 | 60                      | 75                            | 42                           | 8                                | 87  | 3   |
| Shanghai, China            | 2.4                 | 39                      | 87                            | 33                           | 16                               | 88  | 2   |
| Verona, Italy              | 4.6                 | 32                      | 53                            | 36                           | 16                               | 78  | 0   |
| Total                      | 10.1                | 1146                    | 69                            | 50                           | 11                               | 85  | 4   |

\*The definitions of somatization are explained in the Methods section.

tient completed, and a rating of severity on a five-point scale by the treating physician. Each participating center completed translation and back-translation of the diagnostic interview, followed by extensive field testing and reliability testing.<sup>29</sup>

**Analysis of the Data**

Primary analyses, which were limited to patients with a current diagnosis of depressive disorder, examined variations in the probability of somatized depression (according to each of the three definitions described above) among the centers. All comparisons were adjusted for age, sex, educational level, and coexisting medical illness (according to both the physician’s rating of the severity of medical illness and the presence or absence of at least one chronic medical condition checked off by the patient).

Secondary analyses examined specific classifications of the study centers. The first (described by Üstün and VonKorff<sup>34</sup>) involved the type of primary care facility. In this classification, type A centers were characterized by an ongoing relationship between each patient and a personal physician, scheduled appointments, detailed medical records, and careful attention to the privacy of the medical encounter. Type B centers were characterized by a walk-in style of care, without scheduled appointments or ongoing patient–physician relationships. Consultations between patient and physician were typically less private at type B centers than at type A centers. Additional classifications grouped centers according to geographic region (Western Europe and North America vs. Africa, Asia, and South America) and level of economic development (with the use of the United Nations Human Development Index for 1992<sup>35</sup>). Table 1 shows the three classifications. Additional analyses examined patterns of reported symptoms among the patients who were interviewed (those with and those without a current diagnosis of depressive disorder).

**Statistical Analysis**

All analyses are based on symptoms and diagnoses in the month preceding the interview. Although we report the actual

(unweighted) sample size for all analyses, all results incorporate weights to correct for the undersampling of patients with lower scores on the General Health Questionnaire and for nonrespondents at the second-stage assessment.<sup>32</sup> All analyses (linear regression for comparisons of continuous measures and logistic regression for comparisons of categorical measures) were conducted with the use of SPSS for Windows and WesVar Complex Samples software (both from SPSS, Chicago). Because standard statistical software may underestimate variance (and overestimate statistical significance) in studies of stratified samples, the WesVar program was used to calculate variances by means of the jackknife method.<sup>36,37</sup>

**RESULTS**

A total of 1146 patients met the DSM-IV criteria for major depression (weighted prevalence, 10.1 percent) (Table 2). As reported previously,<sup>29</sup> the prevalence of depression varied widely among the centers.

**First Definition of Somatization**

We examined the first definition of somatization (somatic presentation) by comparing the proportion of patients at each center who met the criteria for a depressive disorder and who reported only somatic symptoms as the reason for visiting the physician. As shown in Table 2, this proportion ranged from 45 percent in Paris to 95 percent in Ankara, Turkey (overall prevalence, 69 percent). In a logistic-regression model adjusted for age, sex, educational level, and coexisting medical conditions, the probability of a somatic presentation varied significantly among the centers (P=0.002). According to this definition, the

centers with the highest rates of somatized depression were Ankara, Turkey; Athens, Greece; Ibadan, Nigeria; Bangalore, India; and Shanghai, China. Secondary analyses examined the probability of somatic presentation according to the three classifications of study centers. A somatic presentation was more common in type B centers than in type A centers (odds ratio, 1.8; 95 percent confidence interval, 1.2 to 2.7). This form of somatization did not vary significantly according to the geographic or economic classification of the centers.

### Second Definition of Somatization

We next examined differences among centers according to the second definition of somatization, the reporting of medically unexplained somatic symptoms. The somatization section of the diagnostic interview included 41 such symptoms. To examine the prevalence of somatized depression according to this definition, we computed the proportion of patients with depressive disorder who met the criteria of Kroenke et al.<sup>38</sup> for "multisomatoform disorder" (i.e., at least three unexplained somatic symptoms). This proportion was 50 percent for all the centers combined and exceeded 40 percent at 9 of the 15 centers (Table 2). After adjustment for age, sex, educational level, and coexisting medical conditions, the probability of unexplained somatic symptoms did not vary significantly among the centers ( $P=0.09$ ).

According to the second definition, the centers where depression was most often somatized were Bangalore, India; Groningen, the Netherlands; Rio de Janeiro, Brazil; and Santiago, Chile — the centers with the highest overall rates of reported somatic symptoms. This finding suggests that variation in unexplained somatic symptoms may simply reflect overall differences in symptom reporting (rather than differences in the strength of the relation between depression and unexplained somatic symptoms). To address this issue, we compared the number of unexplained somatic symptoms in patients who had a major depressive disorder with the number in those who did not. The mean ( $\pm$ SD) number of unexplained somatic symptoms reported was  $4.4 \pm 4.2$  among the patients with major depression, as compared with  $1.2 \pm 1.9$  among those without major depression. In a logistic-regression model adjusted for age, sex, and educational level, patients with depression were significantly more likely to report unexplained somatic symptoms than those without depression (odds ratio, 3.5; 95 percent confidence interval, 3.3 to 3.8). The strong relation between depression and unexplained somatic symptoms was a consistent finding among the centers, with center-specific odds ratios ranging from 2.4 to 4.8 ( $P<0.001$  at all centers). This association did not vary significantly with any of the three classifications of study centers.

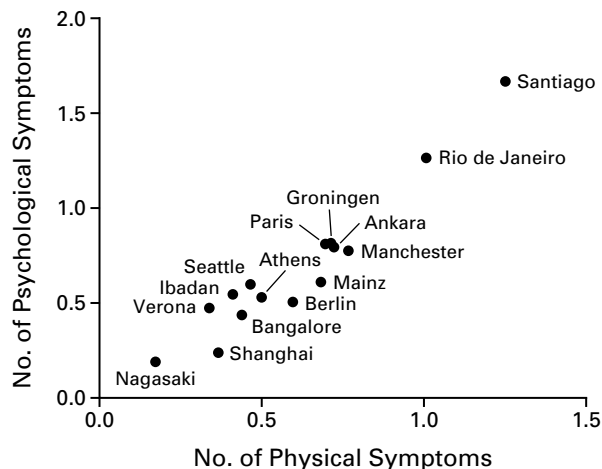
### Third Definition of Somatization

We then examined variation in somatization according to the third definition: denial of psychological symptoms of depression on direct questioning. The diagnostic interview included direct questions about each symptom included in nine DSM-IV criteria for the diagnosis of depression. For each center, we calculated the proportion of patients with major depression who denied the two most overtly psychological symptoms (depressed mood and feelings of guilt or worthlessness) during the diagnostic interview. As shown in Table 2, the overall prevalence was 11 percent, and it did not exceed 26 percent at any center. After adjustment for age, sex, educational level, and coexisting medical conditions, the probability of somatized depression according to the third definition did not vary significantly among the centers ( $P=0.07$ ). The centers where depression was most often somatized were Athens, Greece; Berlin, Germany; Nagasaki, Japan; and Ibadan, Nigeria.

Secondary analyses examined the tendency to deny psychological symptoms among all patients interviewed. Because the prevalence of depressive symptoms varied widely among the centers, we examined the tendency to deny psychological symptoms of depression in relation to the reporting of somatic depressive symptoms (i.e., the relative balance of psychological and somatic symptoms of depression). For these analyses, the nine DSM-IV diagnostic criteria for depression were classified as psychological (depressed mood, loss of interest in activities, impaired concentration, feelings of worthlessness or guilt, and suicidal ideation) or physical (insomnia or hypersomnia, change in weight or appetite, fatigue, and psychomotor agitation or retardation). Figure 1 shows the mean number of psychological symptoms of depression as compared with the mean number of physical symptoms for each center. Although the overall prevalence of depressive symptoms varied greatly among the centers, the balance of psychological and physical symptoms was similar. The tendency to admit or deny psychological symptoms of depression did not vary significantly according to any of the three classifications of study centers.

### Agreement among Definitions

Finally, we examined the extent of agreement among the three definitions of somatized depression (depression with a strictly somatic presentation, depression accompanied by at least three unexplained somatic symptoms, and depression with the denial of psychological symptoms). As shown in Table 2, 85 percent of patients with major depression met at least one of the definitions, but only 4 percent met all three. In none of the three possible comparisons was the agreement between a pair of definitions (as measured by the kappa statistic) greater than that which would be expected by chance. The proportion



**Figure 1.** Mean Numbers of Psychological and Physical Symptoms of Depression at the 15 Study Centers.

Each point represents the mean number of physical symptoms and the mean number of psychological symptoms for primary care patients at a single center. The total sample consisted of 5447 patients. Psychological symptoms were defined as depressed mood, loss of interest in activities, impaired concentration, feelings of worthlessness or guilt, and suicidal ideation. Physical symptoms were defined as insomnia or hypersomnia, change in weight or appetite, fatigue, and psychomotor agitation or retardation.

of patients with major depression who presented with somatic symptoms but acknowledged psychological symptoms when asked about them (i.e., patients who satisfied the first definition of somatized depression but not the third definition) was 60 percent overall and exceeded 40 percent at every center.

## DISCUSSION

The sample of patients at each center was not representative of the regional or national population. Each center attempted to select representative primary care facilities, and the patients enrolled in the study were representative of those seeking care at the facilities. All facilities, however, were located in urban areas, and all patients were seeking care from physicians trained in Western medicine.

Although each definition of somatization that we studied accounted for somatized depression in a substantial number of patients, the agreement among definitions was no greater than one would expect by chance. A similar finding was reported by Kirmayer and Robbins.<sup>16</sup> Given the strong association between psychological distress and somatic symptoms in our study<sup>39</sup> and in other epidemiologic studies,<sup>22,23</sup> poor agreement between the second definition (the reporting of medically unexplained somatic symptoms) and the third (the denial of psychological symptoms) might have been expected. A low level of agreement between different definitions of somatiza-

tion may explain why previous studies (using various definitions and various methods) have reached inconsistent conclusions about cross-national or cross-cultural differences in somatization.

According to our third definition (the denial of psychological symptoms), somatized depression was relatively uncommon at all centers. The data in Figure 1 suggest that patients at different primary care centers differed markedly with respect to the overall likelihood of reporting symptoms of depression but differed little with respect to the reporting of physical symptoms exclusively. The variation among the centers in the proportion of patients with depression who denied psychological symptoms was no greater than the variation that would be expected by chance.

According to our second definition (multiple unexplained somatic symptoms), the somatization of depression was common; the overall prevalence among patients with major depression was 50 percent. The probability of somatized depression according to this definition was similar among the centers. Furthermore, variation among the centers seemed to reflect differences in general rates of symptom reporting rather than any variation in the association between depression and unexplained somatic symptoms. Broader analyses of symptom patterns among all patients interviewed showed strong (and generally similar) associations between depression and unexplained somatic symptoms at every center.

Although somatization as defined on the basis of presenting symptoms had the highest overall prevalence (69 percent), it was the only definition of somatization for which there were significant variations among the centers. The probability of a somatic presentation was significantly greater in the walk-in centers than in those where patients had personal physicians. We cannot, of course, determine whether this observation reflects characteristics of the patients (e.g., "psychological mindedness" or expectations about the scope of primary care), characteristics of the physicians (e.g., training and views about psychological disorders), or the nature of the health care delivery (e.g., the duration of the visit, degree of privacy, and extent of the physician's familiarity with the patient's medical history and life situation).

We should note that the concept of somatization itself rests on the culturally determined assumption that psychological symptoms of depression are more central or primary than somatic symptoms. Our findings suggest that somatic symptoms are a core component of the depressive syndrome. Instead of examining the phenomenon of somatization, we could have studied "psychologization" among depressed patients presenting with primarily psychological symptoms.

We should emphasize the discrepancy between our first and third definitions of somatization: 60 percent of patients with major depression presented with somatic symptoms but acknowledged psychological

symptoms (such as depressed mood or guilt) when specifically asked about them. A similar pattern has been observed in other studies of depression in primary care practice.<sup>18,19,40</sup> The reporting of somatic symptoms may not reflect an unwillingness or inability to acknowledge psychological distress. Instead, patients may believe that the reporting of somatic symptoms is a more appropriate route for seeking help from a primary care physician. Goldberg and Bridges<sup>18,19</sup> have called this process "facultative somatization" and have characterized the initial reporting of somatic symptoms as a "ticket of admission" to the primary care clinic. Thus, without specific questioning, depression and other psychological disorders may not be recognized.

In this report, we have not considered cross-national or cross-cultural differences in the specific somatic symptoms associated with psychological disorders.<sup>41,42</sup> As we reported elsewhere, however, we found no relation between economic development and the types of somatic symptoms associated with psychological distress.<sup>39</sup> We also could not examine differences among centers in the meaning patients attached to symptoms of depression.

Our data provide mixed support for claims about cross-national or cross-cultural differences in somatization. When somatization was defined in terms of patients' reports about symptoms (either denial of psychological symptoms or reporting of medically unexplained somatic symptoms), we found no significant variation in somatization among the study centers — and no evidence of greater somatization in the non-Western or less developed countries. These findings are in agreement with earlier reports that the symptomatic manifestations of depression are similar throughout the world.<sup>13,14,43</sup> When somatization was defined according to presenting symptoms, we found greater variation among the centers, with a greater tendency toward somatic presentations at centers offering walk-in care than at those offering a more personal form of primary care. In other words, the symptomatic experience of depression seems to vary little from one country to another, whereas the interactions between doctors and depressed patients may vary considerably. The somatic presentation of depression or other psychological illness should therefore not be attributed solely to somatization by patients. The definition of legitimate reasons for seeking care reflects the interaction between patients and physicians as well as the structure of the primary care system.

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#### APPENDIX

In addition to the authors, investigators participating in the study of psychological problems in general health care included O. Ozturk and M. Re-

zaki, Ankara, Turkey; C. Stefanis and V. Mavreas, Athens, Greece; S.M. Channabasavanna and T.G. Sriram, Bangalore, India; H. Helmchen and M. Linden, Berlin, Germany; W. van den Brink and B. Tiemens, Groningen, the Netherlands; M. Olawatura and O. Gureje, Ibadan, Nigeria; O. Benkert and W. Maier, Mainz, Germany; R. Gater and S. Kisely, Manchester, United Kingdom; Y. Nakane and S. Michitsuji, Nagasaki, Japan; Y. Lecrubier and P. Boyer, Paris; J.-A. Costa e Silva and L. Villano, Rio de Janeiro, Brazil; R. Florenzano and J. Acuna, Santiago, Chile; H.-Q. Yan and S.F. Xaio, Shanghai, China; and M. Tansella and C. Bellantuono, Verona, Italy. The members of the study advisory group were J.-A. Costa e Silva, D.P. Goldberg, Y. Lecrubier, and H.-U. Wittchen. Members of the coordinating staff at WHO headquarters included N. Sartorius and T.B. Üstün.

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