Medically Unexplained Symptoms in Primary Care

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Fourteen common physical symptoms are responsible for almost half of all primary care visits. Only about 10% to 15% of these symptoms are found to be caused by an organic illness over a 1-year period. Patients with medically unexplained symptoms are frequently frustrating to primary care physicians and utilize medical visits and costs disproportionately. This paper will review the relationship between psychological distress and the decision to seek medical care for common physical symptoms such as fatigue and headache. Evidence will be presented demonstrating that an increasing number of medically unexplained symptoms over a patient's lifetime correlate linearly with the number of anxiety and depressive disorders experienced, the score on the personality dimension of neuroticism, and the degree of functional impairment. Several scales measuring somatization and hypochondriasis are recommended for primary care and medical specialty patients.

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Concern about physical symptoms is the leading reason patients visit primary care physicians, yet only recently have there been methodologically sophisticated investigations into the complex biopsychosocial causes of these symptoms. Although some physical complaints point clearly to underlying disease, others seem to occur in the absence of organic pathology or appear to be expressed in a manner out of proportion to the underlying disease. This paper reviews what is known about physical symptoms that are medically unexplained and how differences in treatment setting, current distress, personality style, and prior family experiences affect the complex process in which individuals interpret and act upon the occurrence of their distressing physical symptoms.

Recent research has demonstrated that physical symptoms are exceedingly common in the general population. Studies of community respondents have all found high prevalence rates of symptoms such as fatigue,[1] headache,[2] and abdominal pain.[3] Population-based surveys[4] have shown that 85% to 95% of community respondents experience at least one symptom every 2 to 4 weeks, and in a health care diary study participants have been shown to have a new symptom every 5 to 7 days.[5] The high prevalence of physical symptoms was demonstrated in the Epidemiologic Catchment Area study,[6] in which the lifetime prevalence of chest pain was 25%, abdominal pain 24%, dizziness 23%, headache 25%, back pain 32%, and fatigue 25%. More than 80% of the time, these symptoms had prompted respondents to see a health care professional, take medication, or reduce normal activities.

Despite the high frequency of these symptoms, however, not all individuals who experience these physical problems bring them to the attention of medical care providers. For example, studies of community respondents with fatigue,[1] migraine headache,[2] and irritable bowel syndrome[3] have all shown that, compared with those who do not seek health care, those who do have either higher scores on measures of psychological distress or are more likely to suffer from a current DSM-III anxiety or depressive disorder. Repeated observations such as these over the last decade have led to six important ideas about the nature of physical symptoms in primary care:

1. The majority of physical symptoms in primary care patients are not associated with an organic disease process.
2. The presence of psychological distress or a psychiatric disorder increases health care utilization and disability, whether or not a physical disease is present.
3. Factors such as early family environment, prior illness experience, and specific personality traits can predispose an individual to develop medically unexplained physical symptoms.
4. There is an association between the number of medically unexplained physical symptoms and the lifetime risk of psychological distress and psychi-

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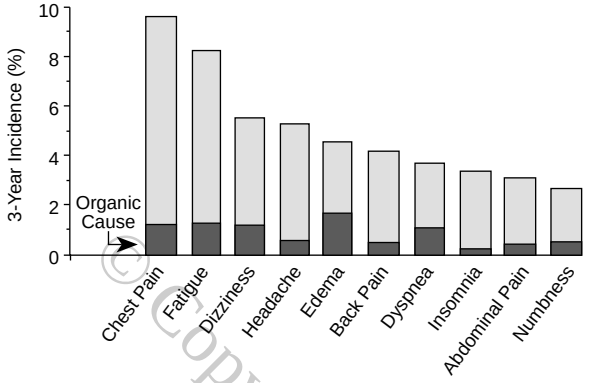
Figure 1. Three-Year Incidence of 10 Common Symptoms in Primary Care: Organic vs. Unexplained Causes*



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atric disorder, and the strength of this relationship increases as patients move into more specialized medical care settings.

5. Medically unexplained symptoms account for a significant percentage of total medical care costs.
6. Medically unexplained symptoms have a major impact on quality of the doctor-patient relationship.

PHYSICAL SYMPTOMS IN PRIMARY CARE

Medically Unexplained Symptoms Are Common in Primary Care

In primary care clinics, 14 common physical symptoms account for approximately 40% of all visits.[7] Kroenke and colleagues showed that, among a large group of primary care patients presenting with one of these 14 symptoms to a general internal medicine clinic, only 10% to 15% were found to have an organic diagnosis that explained the presenting symptom at the end of a 1-year period (Figure 1). Another study[8] has shown that, in 25% to 50% of all primary care visits, no serious medical cause is found to explain the patient complaint. Only 41% of patient problems are clear organic diagnoses, and the most common single diagnosis in primary care is nonsickness.[9] Patients with physical symptoms and no medical diagnosis have often been labeled as the "worried well" by primary care physicians, but a recent study[10] has suggested that these patients have a high prevalence of anxiety and depressive disorders and significant impairment in functioning in their vocational and social lives.

Studies[11,12] over the last 2 decades have shown that 20% to 33% of primary care patients meet criteria for at least one DSM psychiatric disorder. As many as 50% to 70% of these patients initially present to their physician with a physical symptom such as headache or fatigue.[11,13] Primary care studies[11,13] have also shown that misdiagnosis of psychiatric illness occurs approximately 50% of the time, and it is patients with a DSM-IV disorder presenting with a medically unexplained symptom or a complaint about their chronic medical illness who are most likely to be misdiagnosed. Both patients and primary care physicians focus on the physical symptom(s), an emphasis that distracts them from the psychiatric illness.

Although the formal DSM-IV diagnosis of somatization disorder is relatively uncommon in primary care, occurring with a 2% to 5% prevalence rate, less severe forms of somatization are extremely common.[14–16] Patients with common psychiatric diagnoses such as major depression, generalized anxiety disorder, or panic disorder have been shown to have significantly more medically unexplained symptoms than controls without psychiatric illness.[17] In the Epidemiologic Catchment Area (ECA) study,[17] 50% of community respondents with five or more medically unexplained symptoms suffered from a DSM-III psychiatric illness versus only 5% without multiple somatic symptoms. We have also shown that when primary care patients with a new diagnosis of major depression are compared with a population-based control group, over 70% of major depressives have two to five pain complaints that interfere with their lives versus approximately 20% of controls (W. J. K. 1998. Unpublished data).

An abridged form of somatization, termed the Somatic Symptom Index (SSI), has been shown to occur in 10% to 20% of community and primary care respondents.[18] To meet criteria for the Somatic Symptom Index, male patients are required to have four medically unexplained symptoms and female patients six over their lifetimes. This index correlates with high medical utilization and disability, and patients meeting criteria for the SSI have a high prevalence of depressive and anxiety disorders.[18] Based on their research with the 15-item somatic screen questions in the Primary Care Evaluation of Mental Disorders (Prime-MD), Kroenke and colleagues[19] recently proposed a new diagnosis for patients who somatize in primary care. They called this new disorder diagnosis "multisomatoform disorder," and criteria include three or more medical symptoms within the last month that could not be fully explained by a medical disorder. In addition, patients are required to have at least one of these symptoms occur more days than not for 2 or more years and to have accompanying social or vocational disability.[19] Kroenke and colleagues found the multisomatoform disorder to be associated with functional impairment and health care utilization comparable to mood and anxiety disorders.

Unexplained Physical Symptoms Are Frequently Accompanied by Psychiatric Disorders

Three recent studies[10,15,16] have shown that, in large primary care samples, the higher the number of medically unexplained symptoms, the higher the chance of having a current DSM-IV anxiety or depressive diagnosis. We have

also found that, in tertiary care patients with chronic fatigue[20] and primary care patients who were high utilizers of services,[16] there is a significant linear relationship between the number of medically unexplained symptoms patients have experienced over their lifetimes, the number of anxiety and depressive disorders they have experienced currently and over their lifetimes (e.g., major depression, dysthymia, generalized anxiety disorder, panic, agoraphobia), and the degree of current functional impairment. Thus, there is a "dose-response" between the number of unexplained physical symptoms patients experience over their lifetimes and their psychiatric vulnerability.

Approximately one half to two thirds of patients in primary care with a DSM-IV psychiatric illness also have one or more medical illnesses.[11] While psychological distress and psychiatric disorder are associated with physical symptoms in susceptible individuals without known physical disease, they can also amplify aversive symptoms and functional disability in patients with chronic medical disorders.[21] Walker and colleagues[22] have shown that patients who have inflammatory bowel disease (IBD) with a comorbid DSM-IV anxiety and depressive disorder have significantly more gastrointestinal and nongastrointestinal physical symptoms compared with patients who have IBD and no psychiatric illness, despite their having no objective differences in severity of IBD. Similarly, diabetics who have comorbid anxiety and depressive disorders complain of significantly more of the 13 symptoms associated with poor control of diabetes (i.e., polyphagia, polyuria) compared with diabetics without psychiatric illness, despite their having no differences in objective markers of glucose control (i.e., Hb A_{1C}).[23]

Unexplained Symptoms Are Associated With Personality and Psychosocial Factors

The number of medically unexplained symptoms over a patient's lifetime significantly correlates with the degree of neuroticism or harm avoidance.[24] (High scores on these two personality measures correlate with having an Axis II personality disorder.) This association should not be surprising, given the extensive literature on negative affectivity and neuroticism and the experience of bodily symptoms.[24,25–27] Psychologists have shown that patients who have high negative affectivity or neuroticism report a wide range of negative emotions and also tend to score high on measures of physical symptoms.[21,25–27] Patients who score high on these personality measures report more negative life events over time and are more likely to develop an Axis I psychiatric disorder when faced with adverse life events.[21,25–27]

Early childhood maltreatment and adult sexual and physical violence have also been associated with subsequent increases in medical care utilization and physical symptom reporting.[28–30] Although some utilization and symptoms may occur as direct health effects of the victimization (e.g., acute physical trauma or sexually transmitted diseases), more commonly these increases are due to the gradual development of health risk behaviors (i.e., smoking, increased alcohol consumption) and somatization. A substantial literature[28–30] has emerged linking childhood maltreatment and adult assault to several persistent symptom syndromes, such as chronic pelvic pain, irritable bowel syndrome, and fibromyalgia, as well as higher numbers of medically unexplained physical complaints.

Table 1. Medical Specialties and Their Problem Patients*

Orthopedics	Low back pain
Obstetrics and gynecology	Pelvic pain, premenstrual syndrome
Otorhinolaryngology	Tinnitus
Neurology	Dizziness, headache
Cardiology	Atypical chest pain, tachycardia
Pulmonary	Hyperventilation, dyspnea
Dentistry	Temporomandibular joint syndrome
Rheumatology	Fibromyalgia
Internal medicine	Chronic fatigue syndrome
Gastroenterology	Irritable bowel, functional dyspepsia
Rehabilitation	Closed head injury
Endocrinology	Hypoglycemia, labile hypertension
Occupational medicine	Multiple chemical sensitivity

*Adapted from reference 31.

Severity and Number of Symptoms Increase Between Primary and Tertiary Care

Primary care patients who develop more persistent, disabling symptoms often are referred to specialty care clinics. Our research group[31] has also studied several types of aversive, unexplained medical symptoms in specialty clinic patients; we have found that the number and severity of these symptoms as well as related functional disability all increase dramatically compared to primary care samples with similar symptoms. These studies[31] have compared patients experiencing symptoms such as chronic pelvic pain, irritable bowel, or chronic fatigue with patients who have comparable, chronic medical diseases. Our extensive clinical experience in primary care and on the psychiatric consultation liaison service has lead to the description of a subgroup of patients with ill-defined symptoms in each medical specialty who seemed to have high rates of psychiatric disorder on clinical examination (Table 1). We set up a series of case control studies in which a structured psychiatric interview, the Diagnostic Interview Schedule (DIS),[32] was used, and patients had extensive medical work-ups. Thus, in a study of patients with irritable bowel, patients with abdominal pain and other gastrointestinal symptoms were separated into those with irritable bowel and those with inflammatory bowel disease by gastroscopy and colonoscopy results. Patients with chest pain received angiography and were separated into those with and without coronary artery disease. Patients with dizziness were separated by otologic examination and electronystagram into those with and without evidence of peripheral ear disease.

Table 2. Prevalence Rates of Major Depression in Patients With Medically Unexplained Symptoms vs. Controls*

Symptom	Major Depression		Associated Psychiatric and/or Medical Illness in Patients With Medically Unexplained Symptoms
	Current	Lifetime	
Chest pain (CAD+)[a]	35	64	Panic disorder
Chest pain without CAD	3	16	
Pelvic pain	34	66	Substance abuse, sexual abuse
Laparoscopy nonpain controls	10	16	
Tinnitus	60	75	Mild high frequency hearing loss
Hearing-impaired controls	7	15	
Fatigue	15	77	Somatization disorder
Rheumatoid arthritis controls	3	42	
Irritable bowel syndrome	21	61	Panic disorder, somatization disorder
Inflammatory bowel disease controls	6	17	
Fibromyalgia	14	86	Sexual/physical abuse, somatization disorder
Rheumatoid arthritis controls	6	31	
Dizzy without peripheral vestibular disease	12	42	Panic disorder
Controls	5	18	

*Adapted from reference 31. Abbreviation: CAD = Coronary artery disorder.
[a]CAD+ = Angiogram showing 50% or greater stenosis in one or more coronary vessels.

As shown in Table 2, compared with patients who had a chronic medical illness, each of these subgroups of patients with medically unexplained symptoms had significantly higher rates of lifetime major depressive and current major depressive disorder.[31,33,34] Many of these subgroups of patients with medically unexplained symptoms also had higher rates of other associated psychiatric disorders, such as panic disorder or somatization disorder, when compared with medically ill controls. Since patients with medical disorder had significantly lower prevalence rates of major depression in each of these studies, it is unlikely that the affective disorder is secondary to the medical illness in patients with subjective symptoms.

Medically Unexplained Physical Symptoms Are Associated With Increased Costs

Patients having psychiatric illness who present with unexplained physical symptoms or amplification of chronic medical illness symptoms frequently account for high medical costs. Our research group[35] has shown that 10% of primary care patients account for almost one third of outpatient primary care visits, one half of hospital days, one half of specialty visits, and one quarter of prescriptions. We screened over 1000 high utilizers from two primary care clinics and found that approximately 50% had significant psychological distress. Approximately three quarters of these distressed high utilizers had recurrent DSM-IV anxiety and depressive disorders, with a lifetime major depression prevalence of 65%, lifetime generalized anxiety of 40%, lifetime dysthymia of 30%, and lifetime panic disorder of 22%.[35] These distressed high utilizers had a mean of eight to nine medically unexplained symptoms over their lifetimes and 20% met criteria for somatization disorder.[35]

Studies of both young[36] and elderly[37] primary care populations with major depression also have shown that they incur significantly higher medical costs than controls matched for age, gender, and chronic medical illness. The studies have shown that these increases in costs are in all categories—including outpatient visits, laboratory tests, x-rays, inpatient days, and specialty medical visits—not just mental health costs. Moreover, at every level of medical comorbidity, patients with major depression incurred significantly higher overall costs.[37]

Patients with panic disorder have also been shown to have higher medical utilization and medical costs.[38] Due to their presenting somatic complaints and medical signs during anxiety attacks (i.e., tachycardia, hypertension), they frequently receive expensive testing such as Holter monitoring, exercise tolerance tests, and angiograms, pheochromocytoma work-ups, colonoscopy, and gastroscopy, and magnetic resonance imaging scans, computed tomography scans, electroencephalograms, and electronystagmograms. As shown in Table 3, these are costly medical tests.

Medically Unexplained Symptoms and the Doctor-Patient Relationship

Patients with unexplained symptoms who have psychiatric illness are often considered frustrating or difficult by their physicians.[39–41] Studies have shown that 15% to 20% of primary care patients[40] and approximately one third of high utilizers[39] of primary care are considered difficult and frustrating patients, respectively. In one study,[40] 67% of difficult primary care patients versus 35% of nondifficult controls had at least one DSM-III-R mental disorder. In the primary care sample, multisomatiform disorder, panic disorder, dysthymia, generalized anxiety, and major de-

Table 3. Unnecessary Costs of Unrecognized Panic Disorder

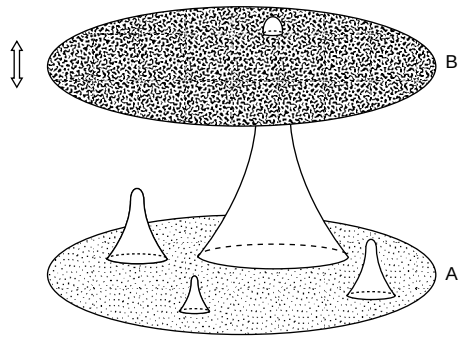
Test	Estimated cost ($)
Chest pain	
Angiography	2000–3000
Echocardiography	350
Treadmill	150
Holter monitor	200
Irritable bowel syndrome	
Gastroscopy	300
Colonoscopy	500
Labile hypertension	
Rule out pheochromocytoma (urinary analysis for catecholamines, vanillymandelic acid, homovanillic acid, and metanephrines)	300
Headache, dizziness	
Magnetic resonance imaging	1000
Computed tomography	550
Electroencephalography	322

pressive disorders had particularly strong associations with difficulty (odds ratios of 12.3, 6.9, 4.2, 3.4, and 3.0 respectively, $p < .001$). Difficult primary care patients had more functional impairment, higher health care utilization, and lower satisfaction with care. In the study of high utilizers of primary care,[39] frustrating high utilizers rated their own health less favorably and reported more somatic symptoms and disabilities than high utilizers who were not rated as frustrating by their physicians. The frustrating patients also had higher health care utilization compared with nonfrustrating patients and, specifically, more emergency room visits. The frustrating high-utilizing patients perceived themselves as more medically impaired than did their physicians.[39] Sharpe and colleagues[41] also found that 22% of patients from two hospital medical specialty clinics and one surgical clinic were considered difficult by their physicians. Difficulty was associated with patient distress, chronic attendance, and less patient satisfaction. Three common types of difficulty were noted: medically unexplained symptoms, coexisting social problems, and severe untreatable illness.[41] Thus, patients with unexplained symptoms and psychiatric illness often take a toll on primary care physicians in terms of their emotional reaction to these patients.

PSYCHOLOGICAL AND PHYSICAL SYMPTOMS: A MODEL

The above data suggest that psychological distress is always accompanied by increased physical symptoms, which seem to occur secondary to autonomic arousal with associated minor somatic symptoms such as increased muscle tension (i.e., headache, backache, and sleep disorder). Sleep disorder itself has been shown to be associated with increased aches and pains. A sleep laboratory study by Muldovsky and Scarisbrick[42] showed that depriving healthy volunteers of Stage 4 sleep for 1 week was associated with the development of a fibromyalgia-like syndrome.

Figure 2. A Model of Symptoms*



*Adapted from reference 43, with permission.

Robinson and Granfield[43] described a schematic model to explain the mechanism by which psychological arousal leads to increased perception of somatic symptoms (Figure 2). In this model, the A axis represents a state of total bodily comfort that rarely occurs. Diary studies[5] have shown that the average person has a new symptom every 5 to 7 days, few of which are brought to a physician's attention.[5] Discomfort experiences that are subthreshold physiologic events stemming from joints, muscles, and internal organs are represented by the bumps on surface A. The height of the bump represents the severity or seriousness of the experience in terms of becoming consciously perceptible. During emotional arousal the A surface becomes increasingly bumpy because of psychophysiologic symptoms such as headache, insomnia, or epigastric pain.[43]

Surface B represents the threshold above which discomfort is consciously perceived. The surface may be driven down by mood and anxiety states, stress, and increased focus of attention. Studies of patients with anxiety and depression suggest that these DSM-IV illnesses tend to lower the B surface, leading to increased worry about and focus of attention on physical symptoms. Successful treatment of anxiety and depressive disorders has been shown to be associated with decreased physical symptom reporting.[44–46]

MEASURING SOMATIZATION

In general, two types of brief questionnaires that measure the tendency to experience and report physical symptoms have been developed. The first type is simply a list of commonly experienced physical symptoms. These questionnaires include lengthy ones such as the Cornell Medical Index[47] and briefer scales such as the Pennebaker Inventory (a 54-item inventory),[25] the Hopkins Symptom Checklist Somatization Scale (a 12-item subscale of the SCL-90R),[48] the 15-item somatization subsection of the Prime-MD,[14] the Bradford Somatic Inventory (a 46-item

scale),[49] and the Modified Symptom Perception Questionnaire (a 13-item Likert scale).[50] All of these scales are valid and reliable instruments in medical patients, with high scores correlating strongly with psychological distress and a higher likelihood of having Axis I disorder. The Prime-MD[14] somatization subsection, in particular, was developed to cover the 15 most common physical symptoms that patients present to primary care physicians (excluding respiratory symptoms). Three or more positive answers out of the first 15 direct the primary care physician to the interview portion of the Prime-MD for somatization disorder. Increasing numbers of these 15 Prime-MD somatic symptoms are correlated with increased risk of an Axis I anxiety or depressive disorder and increased functional impairment.[10]

Several questionnaires have been developed to screen for hypochondriasis. The DSM-IV definition of hypochondriasis emphasizes patients' faulty interpretation of physical sensations as evidence of physical disease and failing to be reassured by the physician that they do not have a serious physical illness, despite often repeated medical examinations and medical tests.[51] Three questionnaires that screen for hypochondriasis include the Whitely Index (a 14-item index scored as "yes" or "no" for each item and devised from the Illness Behavior Questionnaire),[52] the Illness Attitudes Scale (a 29-item questionnaire divided into 9 subscales),[53] and the Somatosensory Amplification Scale (a 10-item Likert scale).[54] In general, all three questionnaires have been demonstrated to have high validity and reliability in medical patients. In addition, the Somatosensory Amplification Scale and the Whitely Index have been shown to be highly correlated with each other.[54] Finally, high scores on the Somatosensory Scale and Whitely Index have been shown to correlate highly with a DSM-IV diagnosis of hypochondriasis established by a structured interview.[54]

There is also a high correlation between scales that measure hypochondriasis and those that measure the tendency to report multiple medically unexplained symptoms. High scores on either type of questionnaire correlate with high numbers of psychological symptoms and a high likelihood of having a comorbid Axis I anxiety or depressive disorder.

CONCLUSION

Patients with medically unexplained symptoms are often frustrating to physicians and utilize a disproportionate share of health care resources. Recent evidence has demonstrated that the number of medically unexplained symptoms a patient experiences is highly correlated with the number of current and lifetime psychological symptoms and psychiatric disorders they have experienced. High numbers of medically unexplained symptoms are also associated with a high risk of an Axis I disorder and high levels of neuroticism and harm avoidance. Several short questionnaires have been developed to screen for both medically unexplained symptoms and hypochondriasis. High scores on these questionnaires suggest the likelihood of the patient's amplifying physical sensations due to psychological distress.

REFERENCES

1. Walker E, Katon WJ, Jemelka RP. Psychiatric disorders and medical care utilization among people in the general population who report fatigue. J Intern Med 1993;8:436–440
2. Stewart WF, Shechter A, Liberman J. Physician consultation for headache pain and history of panic from a population-based study. Am J Med 1992;92(suppl A):353–405
3. Drossman DA, McKee DC, Sandler RS, et al. Psychosocial factors in the irritable bowel syndrome: a multivariate study of patients and non-patients with irritable bowel syndrome. Gastroenterology 1988;95:701–708
4. White K, Williams T, Greenberg B. The ecology of medical care. N Engl J Med 1961;265:885–892
5. Demers RY, Altamore R, Mustin H, et al. An exploration of the dimensions of illness behavior. J Fam Pract 1980;11:1085–1094
6. Kroenke K, Price RK. Symptoms in the community: prevalence, classification, and psychiatric comorbidity. Arch Intern Med 1993;153:2474–2480
7. Kroenke K, Mangelsdorff D. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. Am J Med 1989;86:262–266
8. Barsky AJ, Borus JF. Somatization and medicalization in the era of managed care. JAMA 1995;274:1931–1934
9. Brown JW, Robertson LS, Kusa J, et al. A study of general practice in Massachusetts. JAMA 1971;216;301–306
10. Kroenke K, Spitzer RL, Williams JBW, et al. Physical symptoms in primary care: predictors of psychiatric disorders and functional impairment. Arch Fam Med 1994;3:774–779
11. Bridges KW, Goldberg DP. Somatic presentations of psychiatric disorders in primary care. J Psychosom Res 1987;29:563–569
12. Von Korff M, Shapiro S, Burke JD, et al. Anxiety and depression in a primary care clinic: comparison of diagnostic interview schedule, general health questionnaire, and practitioner assessments. Arch Gen Psychiatry 1987;49:152–156
13. Kirmayer LJ, Robins JM, Dworkind M. Somatization and the recognition of depression and anxiety in primary care. Am J Psychiatry 1993;150: 734–741
14. Spitzer RL, Williams JBW, Kroenke K, et al. Utility of a new procedure for diagnosing mental disorders in primary care: the Prime-MD 1000 study. JAMA 1994;272:1749–1755
15. Gureje O, Simon GE, Ustun TB, et al. Somatization in cross-cultural perspective: a World Health Organization study in primary care. Am J Psychiatry 1997;154:989–995
16. Katon W, Lin E, Von Korff M, et al. Somatization: a spectrum of severity. Am J Psychiatry 1991;148:34–40
17. Simon GE, Von Korff M. Somatization and psychiatric disorder in the NIMH Epidemiologic Catchment Area study. Am J Psychiatry 1991;148: 1494–1500
18. Escobar JI, Golding JM, Hough RL, et al. Somatization in the community: relationship to disability and use of services. Am J Public Health 1987;77: 837–840
19. Kroenke K, Spitzer RL, de Gruy F, et al. Multisomatoform disorder: an alternative to undifferentiated somatoform disorder for the somatizing patient in primary care. Arch Gen Psychiatry 1997;54:352–358
20. Katon W, Russo J. Chronic fatigue syndrome criteria: a critique of the requirement for multiple physical complaints. Arch Intern Med 1992;152: 1604–1609
21. Katon W. The impact of major depression on chronic medical illness. Gen Hosp Psychiatry 1996;18:215–219
22. Walker E, Gelfand MN, Gelfand AN, et al. The relationship of current psychiatric disorder to functional disability and distress in patients with inflammatory bowel disease. Gen Hosp Psychiatry 1996;18:220–229
23. Lustman P, Clouse RE, Carney RM. Depression and the reporting of diabetes symptoms. Int J Psychiatry Med 1988;18:295–303
24. Russo J, Katon W, Sullivan M, et al. Severity of somatization and its rela-

tionship to psychiatric disorders and personality. Psychosomatics 1994;35:546–556
25. Pennebaker J. The Psychology of Physical Symptoms. New York, NY: Springer-Verlag; 1982
26. Watson D, Pennebaker J. Health complaints, stress, and distress: exploring the central role of negative affectivity. Psychol Rev 1989;96:234–254
27. Larsen R, Ketelarr T. Personality and susceptibility to positive and negative emotional states. J Pers Soc Psychol 1991;61:132–140
28. Koss MP, Koss PG, Woodruff WJ. Deleterious effects of criminal victimization on women's health and medical utilization. Arch Intern Med 1991;151:342–347
29. McCauley J, Kern DE, Kolodner K, et al. Clinical characteristics of women with a history of childhood abuse. JAMA 1997;277:1362–1368
30. Walker EA, Katon W. Researching the health effects of victimization: the next generation. Psychosom Med 1996;58:16–17
31. Katon W. The development of a randomized trial of consultation-liaison psychiatry in distressed high utilizers of primary care. Psychiatr Med 1991; 9:577–591
32. Robins LN, Helzer JE, Groughon J, et al. National Institute of Mental Health Diagnostic Interview Schedule: its history, characteristics, and validity. Arch Gen Psychiatry 1981;38:381–389
33. Sullivan M, Clark MR, Katon WJ, et al. Psychiatric and otologic diagnoses in patients complaining of dizziness. Arch Intern Med 1993;153:1479–1484
34. Walker E, Keegan D, Gardner G, et al. Psychosocial factors in fibromyalgia and rheumatoid arthritis, I: psychiatric diagnosis and functional disability. Psychosom Med 1997;59:565–571
35. Katon W, Von Korff M, Lin EHB, et al. Distressed high utilizers of medical care: DSM-III-R diagnoses and treatment needs. Gen Hosp Psychiatry 1990;12:355–362
36. Simon GE, Von Korff M, Barlow W. Health care costs of primary care patients with recognized depression. Arch Gen Psychiatry 1995;52:850–856
37. Unützer J, Patrick DL, Simon GE, et al. Depressive symptoms and the cost of health services in HMO patients aged 65 years and older: a 4-year prospective study. JAMA 1997;277:1618–1623
38. Katon W. Panic disorder: relationship to high medical utilization, unexplained physical symptoms, and medical costs. J Clin Psychiatry 1996;57 (suppl 10):11–18
39. Lin EHB, Katon W, Von Korff M, et al. Frustrating patients: physician and patient perspectives among distressed high users of medical services. J Gen Intern Med 1991;6:241–246
40. Hahn SR, Kroenke K, Spitzer RL, et al. The difficult patient: prevalence, psychopathology, and functional impairment. J Gen Intern Med 1996; 11:1–8
41. Sharpe M, Mayou R, Seagroatt V, et al. Why do doctors find some patients difficult to help? Q J Med 1994;87:187–193
42. Muldovsky H, Scarisbrick P. Induction of neurasthenic musculoskeletal pain syndrome by selective sleep stage deprivation. Psychosom Med 1976; 38:35–44
43. Robinson JO, Granfield AJ. The frequent consulter in primary medical care. J Psychosom Res 1986;30:589–600
44. Noyes R, Clancy J. Reduction in hypochondriasis with treatment of panic disorder. Br J Psychiatry 1986;149:631–635
45. Kellner R, Fava GA, Lisansky J, et al. Hypochondriacal fears and beliefs in DSM-III melancholia: changes with amitriptyline. J Affect Disord 1986; 10:21–26
46. Simon GE, Katon W, Von Korff M, et al. Will improved depression treatment in primary care reduce disability? Psychol Med. In press
47. Brodman K, Erdmann AJ, Wolf HG. Cornell Medical Index Health Questionnaire Manual. New York, NY: Cornell University Medical College; 1956
48. Lipman RS, Covi L, Shapiro AK, et al. The Hopkins Symptom Checklist (HSCL): factors derived from the HSCL-90. Psychopharmacol Bull 1977; 13:43–45
49. Mumford DB, Bovington JT, Hussain KS, et al. The Bradford Somatic Inventory: a multi-ethnic inventory of somatic symptoms reported by anxious and depressed patients in Britain and the Indo-Pakistan subcontinent. Br J Psychiatry 1991;158:379–386
50. Main CJ. The Modified Symptom Perception Questionnaire (MSPQ). J Psychosom Res 1983;27:503–514
51. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
52. Pilowsky I. Dimensions of hypochondriasis. Br J Psychiatry 1967;113: 89–93
53. Kellner R, Abbot P, Winslow WW, et al. Fears, beliefs and attitudes on DSM-III hypochondriasis. J Nerv Ment Dis 1987;175:20–25
54. Barsky AJ, Wyshak G, Klerman GL. The Somatosensory Amplification Scale and its relationship to hypochondriasis. J Psychiatr Res 1990;24: 323–334

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