

Patterns and Correlates of Generalized Anxiety Disorder in Community Samples

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Background: Although generalized anxiety disorder (GAD) is at least twice as prevalent as panic disorder and is among the commonly occurring mental disorders, changing diagnostic criteria have hampered the cumulation of data on patterns and correlates. **Method:** A computer literature search was carried out for the terms *generalized anxiety disorder* and *GAD* in the MEDLINE and PsycLIT databases. Reports published in English since 1995 were reviewed to determine patterns and correlates of GAD in the general population. **Results:** The literature shows clearly that GAD is a commonly occurring disorder associated with serious impairment. Although the high comorbidities of GAD with other disorders in clinical samples led to speculation that the impairments associated with GAD were due to comorbid conditions, several recent studies show that pure GAD is associated with serious impairments. Considerable uncertainty remains regarding appropriate diagnostic criteria. The requirements that the anxiety be excessive and persist for 6 months are the subject of the most controversy. Recently reported community epidemiologic data show that generalized anxiety syndromes that persist for shorter time periods and that are not excessive in relation to objective stressors are as seriously impairing as syndromes that meet full criteria for GAD. It is less clear whether currently available treatments are as useful in resolving episodes of generalized anxiety that lie outside the boundaries of current ICD and DSM criteria. **Conclusion:** GAD is a commonly occurring mental disorder that can seriously impair functioning. Coordinated community epidemiologic studies and treatment effectiveness studies are needed to resolve remaining uncertainties regarding the diagnostic boundaries of GAD. (J Clin Psychiatry 2002;63[suppl 8]:4-10)

Generalized anxiety as a “disorder” (GAD) was first officially recognized over 2 decades ago in the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition (DSM-III).¹ A good deal of information on the prevalence, correlates, and treatment response of the disorder has been generated over the intervening years. However, this evidence is less extensive than it might otherwise be since cumulation of these data has been hampered by the important changes in the diagnostic criteria of

GAD that have been introduced twice during the intervening years, first in DSM-III-R² and then again in DSM-IV.³ An additional complication is that criteria for GAD in the DSM system differ from criteria in the World Health Organization (WHO) *International Classification of Disease*, Tenth Edition (ICD-10).⁴ To review the patterns and correlates of GAD in the general population, we conducted a computer literature search of MEDLINE and PsycLIT databases using the terms *generalized anxiety disorder* and *GAD*. Reports published in English since 1995 were reviewed.

Despite the changes in diagnostic criteria, there is now good agreement that the core symptoms of GAD are persistent psychological anxiety, nervousness, or worry that continue over time and that are to some extent uncontrollable—that is, severe enough that the person cannot put these symptoms out of mind at will.⁵ The anxiety must also be accompanied by somatic symptoms that have been found empirically to co-occur with clinically significant persistent anxiety, although the ICD system places greater emphasis than the DSM system on these somatic symptoms. Another requirement is that the anxiety must be excessive—that is, substantially greater than might be expected on the basis of the person’s objective life circumstances. However, there is controversy over this criterion that is discussed later in this

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article. A final requirement is that the syndrome must persist most days for a minimum of 6 months. We discuss the controversy about this requirement below.

A great deal of debate has gone on concerning the nosological status of GAD from the time the diagnosis was first introduced in DSM-III. This controversy was initially based on reports of low diagnostic reliability using standard criteria⁶ and on the fact that early clinical studies of DSM-III GAD found that the vast majority of patients with the disorder also met criteria for some other anxiety or mood disorder, with an especially strong comorbidity between GAD and major depression.^{7,8} This high comorbidity led some commentators to suggest that GAD might be better conceptualized as a prodrome or residual or severity marker of depression than as an independent disorder.⁹⁻¹¹ This concern motivated a change in the 1-month minimum duration requirement for GAD in DSM-III to a 6-month requirement in DSM-III-R, ICD-10, and DSM-IV based on the observation that the comorbidity of GAD with other disorders decreases as the duration of GAD increases.¹²

An issue of special importance in the evaluation of whether GAD is a distinct disorder rather than a prodrome or residual or severity marker is whether the symptoms of GAD form an empirical cluster that is distinct from the symptoms of other disorders, especially depression, in representative samples.¹³ Brown and colleagues¹⁴ investigated this issue in a comparison of the symptoms of GAD with major depression. Their analysis shows clearly that there are separate latent factors of positive affectivity, negative affectivity, and autonomic suppression (related to GAD), strongly arguing that GAD and major depression can be distinguished despite the overlap of some core symptoms. Maier and colleagues¹⁵ evaluated a related issue in the WHO study on Psychological Problems in Primary Care, in which they found that the associated psychophysiologic symptoms of GAD specified in ICD-10 do, in fact, strongly cluster with the core symptoms of persistent worry and anxiety.

PREVALENCE

Despite variation in the diagnostic criteria of GAD used in published prevalence studies, the reported lifetime prevalence rates of GAD are fairly consistent in the epidemiologic literature when the 6-month duration requirement is used. Prevalence estimates for adults in community epidemiologic surveys are between 1.5% and 3% for current GAD, 3% to 5% for GAD in the past year, and 4% to 7% for lifetime GAD.¹⁶⁻²⁰ Many fewer data exist on prevalence estimates among children and adolescents. However, the prospective Early Developmental Stages of Psychopathology study of adolescents and young adults, the largest and most recent survey of DSM-IV disorders among young people, found that, according to the strict DSM-IV criteria, GAD is rare in children and adolescents.²¹

The low prevalence of GAD among young people is quite different from the pattern for other anxiety disorders, which typically start early in life and have high prevalences among adolescents and young adults. Retrospectively reported age at onset data obtained from community cases of GAD suggest another important difference from other anxiety disorders: that the upper end of the age range associated with high risk of GAD onset is much older for GAD (mid-50s) than for other anxiety disorders.²²⁻²⁵ It is not clear why this is the case, but one plausible possibility is that chronic stressors that occur throughout the life course are more likely to trigger first onset of GAD than of other anxiety disorders. We are aware of no comparative research on the predictors of first onset of GAD and other anxiety disorders. Such research would be useful to help understand this important difference in age at onset distributions.

There is much less evidence regarding the age at onset of GAD when the DSM-III 1-month duration requirement is used. This lack is unfortunate because, as discussed in more detail below, there is good reason to believe that the 1-month duration requirement is more valid than the 6-month requirement.²⁶ The limited available evidence on the prevalence of 1-month GAD suggests that current prevalence would more than double if the duration requirement was reduced from 6 months to 1 month.^{15,27} However, it is not known how age at onset would be affected by such a change in the duration requirement. It seems likely that estimated age at onset would decrease, perhaps dramatically so, if this change was implemented. This prediction is based on empirical evidence that anxious temperament, which begins early in life,²⁸ underlies many cases of GAD.^{29,30} Current thinking about this interplay is that acute episodes of anxiety occur among people with anxious temperament in response to situational triggers.³¹ If these acute episodes increase in duration over time, as they well might,³² then first onset of generalized anxiety defined in terms of comparatively short, but clinically significant, episodes might well be at a much earlier age than first onset of an episode that persists for 6 months.

A number of primary care studies have estimated the prevalence of GAD among patients visiting their family doctors.^{33,34} The largest of these, the international WHO study of Psychological Problems in General Health Care (PPGHC),³⁵ found that 8% of primary care attendees in participating countries met criteria for current GAD at the time of visiting the doctor. This was the highest prevalence of any anxiety disorder found in this sample. In a subsample study of 5 European centers that participated in PPGHC, 8.5% of attendees met full criteria for GAD and an additional 4.1% met subthreshold criteria.³⁵ The most recent primary care study to examine GAD was carried out in conjunction with a single day of screening over 20,000 patients in more than 500 primary care centers.³⁶⁻³⁹ This study reported a point prevalence of GAD of 5.3% and, like the PPGHC study, found that GAD was the most commonly

occurring anxiety disorder in primary care, with more than 50% of the patients with any anxiety disorder meeting criteria for GAD. The PPGHC study also found that the number of patients meeting subthreshold criteria for GAD was greater than the number meeting full criteria.¹⁵ A similar result has been reported in other primary care studies. For example, Olfson and colleagues²⁷ found that 6.6% of patients in a primary care sample met subthreshold criteria for GAD compared with 3.6% who met full criteria.



COURSE

Retrospective reports about the course of GAD based on epidemiologic surveys^{16,40} and clinical studies^{41,42} suggest that GAD is a chronic condition, with episodes commonly persisting for a decade or longer. The small amount of prospective data on the course of GAD is consistent with these retrospective estimates. The richest prospective data of this sort come from the Harvard/Brown Anxiety Disorder Research Program (HARP),^{43,44} a prospective naturalistic study of patients with anxiety disorders followed at 6-month intervals for 2 years and annually thereafter to observe the natural history of their disorders. Only 15% of HARP respondents with baseline GAD had a full remission for 2 months or longer at any time in the first year after baseline, while only 25% had a full remission in the 2 years after baseline,⁴⁴ and only 38% had a full remission after 5 years.⁴⁵

As one might expect the course of GAD to be more persistent among patients in treatment than in the general population, it is noteworthy that data on the chronicity of GAD obtained in the Epidemiologic Catchment Area (ECA) study, a large general population survey, are consistent with the HARP study in showing that the duration of DSM-III GAD is typically quite chronic.¹⁶ It is not clear whether estimates of chronicity would change if the criteria for GAD were modified to require a 1-month rather than a 6-month minimum duration. The estimated chronicity of cases that meet the current 6-month duration requirement would, by definition, either stay the same or increase. It is likely that the chronicity of cases that fail to meet current ICD or DSM criteria is lower. However, if the definition of GAD was broadened to include cases with a pattern of recurrent episodes that persist for at least 1 month—a definition consistent with the conceptualization of GAD as a situationally triggered acute phase of a temperamental style^{30,31}—then the chronicity of this acute phase might well be as high as the chronicity of ICD-10 and DSM-IV GAD.

Sociodemographic Correlates of Onset and Course

GAD is more commonly found among women than men and among people of various disadvantaged social statuses (e.g., low income and education, racial-ethnic minorities) compared with their more socially advantaged

counterparts.^{16,18,46} However, prospective analyses show that none of these sociodemographic variables is a significant predictor of the course of GAD.^{45,47} Age has a much more complex relationship than other sociodemographic variables with GAD. The highest current prevalence of GAD is found among people in the middle years of life.¹⁸ This is attributable to the joint occurrence of significant cohort effects overlaid on differential recurrence risk as a function of age. The cohort effect, inferred from retrospective age at onset reports, suggests that the lifetime prevalence of GAD has been on the rise in successive cohorts born over the past half century. Once onset occurs, though, risk of current prevalence is inversely related to age but not to age at onset. Consequently, the highest current prevalence is in the middle years of life due to a comparatively high lifetime risk (cohort effect) and a comparatively low rate of remission.

COMORBIDITY

As noted in the introduction, the high comorbidity of patients with DSM-III GAD documented in early clinical studies led to an increase in the duration requirement from 1 month in DSM-III¹ to 6 months in subsequent editions of the DSM and ICD-10. Despite this change, the rates of comorbidity with depression and other common mental disorders among patients in treatment for GAD remain high today.^{48,49} The most common comorbid conditions in addition to major depression are panic disorder, social and specific phobia, and posttraumatic stress disorder (PTSD).⁵⁰ It is important to appreciate, though, that the evidence of high comorbidity is based on clinical samples. Studies of community samples show that most comorbidities are not more common in GAD than in other anxiety or mood disorders, although GAD continues to have a very high comorbidity with major depression even in community samples.¹⁸ The higher comorbidity of GAD in clinical samples compared with community samples is due to the fact that comorbidity is a powerful predictor of help-seeking among people with GAD, leading to an especially high rate of comorbidity among people with GAD who seek treatment for their emotional problems.¹⁸

The high comorbidity of GAD in clinical samples can be interpreted in at least 2 ways. First, pure GAD might not be seriously impairing in itself, so that only when GAD co-occurs with other anxiety or mood disorders does the level of distress in GAD motivate people with the disorder to seek treatment. If this is the case, it could be argued that GAD may be an independent disorder, but that it is only clinically significant when it is part of a comorbid cluster in which the comorbid disorders should be the focus of clinical attention. Second, people with GAD, although they worry about a great number of things, might not perceive their worrying to be a problem in the absence of other comorbid disorders more easily recognized as pathologic.

The distinction between these 2 possibilities is of considerable importance in evaluating whether GAD should be considered a clinically significant disorder in its own right. This issue has been examined indirectly by studying the impairments associated with pure and comorbid GAD in the community. The consistent finding is that the impairments associated with pure GAD (i.e., GAD in the absence of any other commonly occurring mental disorder) are as great as, and in many cases greater than, the impairments associated with other common mental disorders.^{17,33,34,51} This finding is inconsistent with the argument that the low treatment rates for pure GAD are due to lower impairments than those caused by other psychiatric disorders.

PREDICTIVE PRIORITIES

One interesting way to study the implications of comorbidity is to investigate prediction: whether one disorder in a particular pair, when it starts at an earlier age, is a significant predictor of the subsequent first onset of the other disorder. This was examined in the National Comorbidity Survey (NCS), a nationally representative survey of the U.S. household population.⁵² The analysis used retrospective age at onset reports to estimate a series of bivariate survival models in which prior onset of one disorder was treated as a time-varying covariate of another disorder. All temporally primary anxiety and mood disorders were statistically significant predictors of the subsequent first onset of other anxiety and mood disorders. GAD did not stand out in any particular way in comparison with the other disorders, either in magnitude of effects in predicting later disorders, or in the magnitude of effects of other disorders in predicting first onset of GAD. This means that any questions regarding the validity of GAD as a diagnostic entity on the basis of data about comorbidity would apply equally to major depression, panic disorder, social phobia, and all the other anxiety and mood disorders considered in this analysis.

Another interesting line of analysis involving comorbidity focuses on severity and course. Kessler⁵³ reviewed whether comorbidity is associated more strongly with the severity or course of GAD than other anxiety or mood disorders in the NCS. The rationale was that, if GAD is nothing more than a prodrome or residual or severity marker of other disorders, the severity and course of GAD would be much more strongly affected by comorbidity than would the severity and course of other anxiety or mood disorders. The results showed clearly that this is not the case. Comorbidity is generally associated with increased severity and persistence for all anxiety and mood disorders. The patterns involving GAD in the NCS were generally similar to those for other disorders.

There was one important exception to this general pattern in the NCS analysis: GAD was the only anxiety or mood disorder in which persistence, as indirectly indicated by recency controlling for age at onset and time since

onset, was unrelated to comorbidity.⁵⁴ It is conceivable that this unique effect of GAD—which is based entirely on retrospective reports in the NCS analysis—is due to a retrospective recall bias associated with the greater chronicity of GAD compared with other anxiety or mood disorders. However, contrary to this assumption, Yonkers and colleagues⁴⁵ reported a similar result in a prospective analysis of the HARP study. Yonkers and colleagues found that the course of comorbid GAD is unrelated to whether the GAD is primary or secondary and that this pattern was quite different from the pattern found for other anxiety disorders in the HARP data.²⁵ This consistent result means that, if anything, GAD behaves more like an independent disorder in this respect than do other anxiety or mood disorders.

IMPAIRMENTS

It was noted in the section on comorbidity that pure GAD is as impairing as pure depression. No mention was made, however, of just how severe these impairments are. Analyses of 2 U.S. national surveys examined one aspect of this issue by asking respondents about sickness, absence from work, and other days out of role during the 30 days before the interview.^{55,56} Responses were related to information obtained in the surveys about chronic physical and mental disorders. In bivariate analyses, GAD was found to be associated with a larger number of days out of role than any other condition except cancer, with an average of 4 such days per month reported for the typical GAD sufferer. The rank ordering of GAD fell in multivariate analyses due to the fact that some of the impairment associated with having GAD was a consequence of comorbid disorders. However, even in the multivariate analyses, GAD was ranked among the 10 most impairing chronic conditions in terms of days out of role, with a typical level of impairment comparable with that associated with arthritis, diabetes, and ulcers.

The PPGHC study of primary care attendees found results very similar to those in the NCS general population sample. Patients with GAD in the PPGHC samples were more impaired than patients with the vast majority of other chronic conditions.⁵⁷ Importantly, the PPGHC studied not only days out of role, but also a number of more subtle measures of impairments in daily social and productive role functioning, and found that the adverse effects of GAD can be found across the full range of these impairment dimensions. The German Health Survey found similar results in a nationally representative sample of the general population that used physical examinations and record checks to confirm reports of having chronic conditions.⁵⁸ Similar results using self-reports were also found in a national survey in Australia, where only cancer and heart disease had higher levels of impairment than GAD.⁵⁹

Research has also been done on the long-term impairments of GAD. As noted above, GAD is a significant

predictor of the subsequent onset of other anxiety and mood disorders. It is not clear whether these predictive associations are causal. However, if this is so, then secondary disorders should be considered to be adverse consequences of unremitting GAD. Retrospective analyses of the NCS data have also shown that early-onset GAD significantly predicts school failure,⁶⁰ teenage childbearing,⁶¹ and marital failure.⁶² A long-term prospective study of the adult consequences of anxiety and depression in adolescence replicated and extended the NCS results to show that early-onset GAD predicts a wide range of adverse adult outcomes in social and productive roles.⁶³

HEALTH CARE UTILIZATION

We noted earlier in the article that studies in primary care samples consistently find that GAD is a common condition among primary care attendees.³³⁻³⁸ According to the most recent primary care study, people with GAD make twice as many visits to primary care doctors as other primary care patients with the same sociodemographic characteristics and similarly chronic physical conditions.³⁷ In addition, because of the active help-seeking associated with health concerns among people with GAD, the prevalence of GAD is even higher in specialty health care clinics than in primary care settings. Gastroenterology seems to be the most frequently consulted specialty area. Indeed, one study found that twice as many people with GAD can be found in treatment with a gastroenterologist as in treatment with a psychiatrist,⁶⁴ presumably due to the overlap of somatic symptoms of GAD with those of gastrointestinal disorders.

Despite this high rate of help-seeking, only a minority of people with GAD seek help for their emotional problems. Indeed, one study found that even though the vast majority of people with GAD see a doctor every year, fewer than one third of them discuss their emotional problems during any of these visits.⁵⁰ It is not difficult to understand why this is so. People with GAD are excessive worriers, and health problems, either imagined or real, are often one focus of their worries. However, because their worry is focused on their health, they seldom recognize that the worry itself is a source of concern. It is often only when the worry is accompanied by panic attacks or serious depression that these people come to realize that their persistent worrying is pathologic and that they need help. Consequently, help-seeking for GAD is usually a late response to the disorder, with the typical interval between first onset of GAD and first contact with the treatment system for help with the disorder estimated to average more than a decade.^{65,66}

Given that people with GAD are heavy users of primary care services, one potentially effective approach to increase detection and utilization would be to develop screening programs in primary care. A pilot study of this

sort carried out in Germany found that the vast majority of primary care patients are willing to complete a GAD screening questionnaire in the waiting room before seeing their doctor.³⁶⁻³⁸ Moreover, such a screening questionnaire can accurately detect GAD, and patients with GAD who are detected in this way are willing to accept treatment for their anxiety even though they generally came to the doctor with a different presenting complaint.³⁶⁻³⁸ A critical unresolved question, though, is whether primary care physicians can be motivated to implement routine GAD screening. An enormous impediment to doing this is the fact that primary care doctors are now being pressured to screen for a wide variety of undertreated illnesses by advocacy groups for these separate illnesses. It is impossible to administer all of these screening questionnaires in the absence of an integrated administration and scoring system. Although systems of this sort have been developed, their use to date has been limited by the realization that detection and treatment of all these currently undetected illnesses could swamp the resources of the primary care physician. It is unclear how this situation will be resolved, but it is unlikely that routine screening for GAD in primary care will become a reality until this resolution occurs.

UNRESOLVED ISSUES

We noted earlier in the article that controversy continues to exist about the diagnostic criteria for GAD. The most important aspect of this controversy involves the 6-month duration requirement. It is now clear that this requirement excludes a substantial number of people who have clinically significant and chronic recurrent generalized anxiety. It is also clear, based on recent taxometric analyses, that a dimensional model of generalized anxiety is more consistent with the data than a model that assumes the existence of a true latent disorder that can be discriminated from "normal" worry only after a duration of 6 months.⁶⁷

The "correct" criteria for GAD, of course, depend on the purposes at hand. The optimal criteria for maximizing estimates of heritability in genetic studies, for example, might be quite different from those applied in defining the subset of anxious people likely to respond to a particular type of treatment. These sets of criteria, in turn, might differ from the optimal criteria for determining how many people suffer from anxiety that is serious enough to interfere with role functioning. If the latter criteria are taken as the most appropriate ones for defining clinical significance, though, then the evidence is clear that the current ICD and DSM criteria are overly restrictive.¹⁵

Another aspect of the GAD diagnosis controversy is the requirement that psychological anxiety must be excessive to qualify for a diagnosis of GAD. This means that people who suffer from clinically significant anxiety during exposure to life situations that would lead most people to be very anxious are defined as not having a mental illness unless

their anxiety leads to some other qualifying disorder such as panic attacks, PTSD, or adjustment disorder. It is interesting to note that there is no comparable requirement that dysphoria must be excessive to qualify as major depression. Recent epidemiologic research has shown that the people who meet all the diagnostic criteria for GAD other than the requirement that their anxiety is excessive are very similar to people who meet all GAD criteria in terms of a number of external validators.⁶⁸ Preliminary data suggest that elimination of the “excessiveness” criterion would lead to a substantial increase in the number of people in the general population who meet diagnostic criteria for GAD.

Another unresolved issue concerning diagnosis is that difficulties persist in applying the diagnostic criteria for GAD, despite the efforts of the American Psychiatric Association to refine them. Universal application of the criteria is difficult because of cultural differences between nations both in the ways patients perceive and describe their internal subjective states, as well as in their standards for defining worries as “excessive.” In addition, language barriers impede translation of subjective terms such as “worry” and “apprehensive expectation.” Remaining differences between the DSM and ICD systems exacerbate these other problems. While the current DSM criteria place greater emphasis on psychological symptoms and lack of ability to control anxiety, somatic symptoms play a more prominent part in the ICD system. Finally, as noted earlier in the article, patients with GAD typically present with complaints about other physical and/or emotional problems, making it necessary for clinicians to be vigilant if they are to detect GAD.⁶⁹ In the course of being vigilant, however, clinicians also need to be aware that patients who have serious physical illnesses will understandably have associated anxieties. It is consequently important to obtain information on the objective basis for anxiety in order to avoid overdiagnosis.

The ultimate utility of diagnostic distinctions is to guide treatment decisions. As a result, future naturalistic studies of variation in GAD diagnostic criteria need to be carried out in coordination with clinical studies in order to be optimally useful. Only in this way will we be able to evaluate the relative effectiveness of treatments across disorder subtypes. It is important that such future studies are implemented in representative community samples, rather than in samples of help-seekers, in order to yield unbiased evidence regarding population distributions of disorder subtypes and treatment response. There is already emerging literature that is examining aspects of such subtypes in clinical samples. Perhaps the most interesting result of these studies is that currently available pharmacologic treatments of GAD are more effective in resolving acute symptoms than in modifying the anxious temperament and inability to cope with uncertainty that often underlie these symptoms.⁷⁰ This result raises the interesting, but as yet unexamined, question of whether psychological treatments might be more effective than pharmacologic treatments in altering the tem-

peramental underpinnings of GAD.²⁶ If so, the next logical question is whether early psychological treatment of youths with anxious temperaments might delay or prevent the onset of GAD or alter the course of the disorder once it occurs. All of these questions need to be addressed in representative samples that expand the evaluation and treatment of generalized anxiety in the ways discussed above, going beyond the current diagnostic criteria for GAD.

REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition. Washington, DC: American Psychiatric Association; 1980
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition, Revised. Washington, DC: American Psychiatric Association; 1987
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
4. World Health Organization. *The International Classification of Diseases, 10th Revision: Classification of Mental and Behavioral Disorders: Diagnostic Criteria for Research*. Geneva, Switzerland: World Health Organization; 1990
5. Ballenger JC, Davidson JRT, Lecrubier Y, et al. Consensus statement on generalized anxiety disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry* 2001;62(suppl 11):53–58
6. Di Nardo P, Moras K, Barlow DH, et al. Reliability of DSM-III-R anxiety disorder categories: using the Anxiety Disorders Interview Schedule-Revised (ADIS-R). *Arch Gen Psychiatry* 1993;50:251–256
7. Breier A, Charney DS, Heninger GR. The diagnostic validity of anxiety disorders and their relationship to depressive illness. *Am J Psychiatry* 1985;142:787–797
8. Breslau N. Depressive symptoms, major depression and generalized anxiety: a comparison of self-reports on CES-D and results from diagnostic interviews. *Psychiatry Res* 1985;15:219–229
9. Breslau N, Davis GC. Further evidence on the doubtful validity of generalized anxiety disorder [letter]. *Psychiatry Res* 1985;16:177–179
10. Clayton PJ, Grove WM, Coryell W, et al. Follow-up and family study of anxious depression. *Am J Psychiatry* 1991;148:1512–1517
11. Noyes R Jr, Woodman C, Garvey MJ, et al. Generalized anxiety disorder vs panic disorder: distinguishing characteristics and patterns of comorbidity. *J Nerv Ment Dis* 1992;180:369–379
12. Breslau N, Davis GC. DSM-III generalized anxiety disorder: an empirical investigation of more stringent criteria. *Psychiatry Res* 1985;15:231–238
13. Robins E, Guze SB. Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia. *Am J Psychiatry* 1970;126:983–987
14. Brown TA, Chorpita BF, Barlow DH. Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *J Abnorm Psychol* 1998;107:179–192
15. Maier W, Gansicke M, Freyberger HJ, et al. Generalized anxiety disorder (ICD-10) in primary care from a cross-cultural perspective: a valid diagnostic entity? *Acta Psychiatr Scand* 2000;101:29–36
16. Blazer DG, Hughes D, George LK, et al. Generalized anxiety disorder. In: Robins LN, Regier DA, eds. *Psychiatric Disorders in America*. New York, NY: The Free Press; 1991:180–203
17. Kessler RC, Dupont RL, Berglund P, et al. Impairments of twelve-month independent and comorbid generalized anxiety disorder and major depression in two national surveys. *Am J Psychiatry* 1999;156:1915–1923
18. Wittchen H-U, Zhao S, Kessler RC, et al. DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. *Arch Gen Psychiatry* 1994; 51:355–364
19. Bijl RV, Ravelli R, van Zessen G. Prevalence of psychiatric disorder in the general population: results of the Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Soc Psychiatry Psychiatr Epidemiol* 1998; 33:587–595
20. Offord DR, Boyle MH, Campbell D, et al. One-year prevalence of psychiatric disorder in Ontarians 15 to 64 years of age. *Can J Psychiatry* 1996;41: 559–563

21. Wittchen H-U, Nelson CB, Lachner G. Prevalence of mental disorders and psychosocial impairments in adolescents and young adults. *Psychol Med* 1998;28:109–126
22. Burke KC, Burke JD Jr, Rae DS, et al. Comparing age at onset of major depression and other psychiatric disorders by birth cohorts in five US community populations. *Arch Gen Psychiatry* 1991;48:789–795
23. Kendler KS, Neale MC, Kessler RC, et al. Generalized anxiety disorder in women: a population-based twin study. *Arch Gen Psychiatry* 1992;49:267–272
24. Barlow DH, Blanchard RB, Vermilyea JA, et al. Generalized anxiety and generalized anxiety disorder: description and reconceptualization. *Am J Psychiatry* 1986;143:40–44
25. Rogers MP, Warshaw MG, Goisman RM, et al. Comparing primary and secondary generalized anxiety disorder in a long-term naturalistic study of anxiety disorders. *Depress Anxiety* 1999;10:1–7
26. Rickels K, Rynn MA, Khalid-Khan S. Diagnosis and evaluation of generalized anxiety disorder (GAD) patients. In: Nutt D, Rickels K, Stein D, eds. *Generalised Anxiety Disorder: Symptomatology, Pathogenesis and Management*. London, England: Martin Dunitz. In press
27. Olfson M, Broadhead WE, Weissman MM, et al. Subthreshold psychiatric symptoms in a primary care group practice. *Arch Gen Psychiatry* 1996;53:880–886
28. Kagan J, Snidman N. Early childhood predictors of adult anxiety disorders. *Biol Psychiatry* 1999;46:1536–1541
29. De Beurs E, Beekman AT, Deeg DJ, et al. Predictors of change in anxiety symptoms of older persons: results from the Longitudinal Aging Study Amsterdam. *Psychol Med* 2000;30:515–527
30. Dugas MJ, Gagnon F, Ladouceur R, et al. Generalized anxiety disorder: a preliminary test of a conceptual model. *Behav Res Ther* 1998;36:215–226
31. Akiskal HS. Toward a definition of generalized anxiety disorder as an anxious temperament type [review]. *Acta Psychiatr Scand Suppl* 1998;393:66–73
32. Starcevic V, Bogojevic G. The concept of generalized anxiety disorder: between the too narrow and too wide diagnostic criteria. *Psychopathology* 1999;32:5–11
33. Ormel J, Von Korff M, Ustun TB, et al. Common mental disorders and disability across cultures: results from the WHO Collaborative Study on Psychological Problems in General Health Care. *JAMA* 1994;272:1741–1748
34. Schonfeld WH, Verboncoeur CJ, Fifer SK, et al. The functioning and well-being of patients with unrecognized anxiety disorders and major depressive disorder. *J Affect Disord* 1997;43:105–119
35. Ustun TB, Sartorius N, eds. *Mental Illness in General Health Care: An International Study*. Chichester, NY: John Wiley & Sons; 1995
36. Wittchen H-U, Linden M, Schwarzer W, et al. Generalisierte Angststörungen (GAS) – Ein vernachlässigtes Krankheitsbild? Hintergrund und Zielsetzung der GAD-P Studie. *Münchener Medizinische Wochenschrift Sonderheft* 2001;1:1–4
37. Wittchen H-U, Krause P, Hoyer J, et al. Prävalenz und Korrelate Generalisierter Angststörungen in der Allgemeinarztpraxis. *Münchener Medizinische Wochenschrift Sonderheft* 2001;1:17–25
38. Hoyer J, Krause P, Höfler M, et al. Wann und wie gut erkennt der Hausarzt Generalisierte Angststörungen und Depressionen? *Münchener Medizinische Wochenschrift Sonderheft* 2001;1:26–35
39. Wittchen H-U, Hoyer J, Beesdo K, et al. Probleme und Defizite in der hausärztlichen Versorgung von Generalisierten Angststörungen. Konsequenzen der GAD-P-Studie und Prioritäten für eine verbesserte Versorgung. *Münchener Medizinische Wochenschrift Sonderheft* 2001;1:42–49
40. Angst J, Vollrath M. The natural history of anxiety disorders [review]. *Acta Psychiatr Scand* 1991;84:446–452
41. Mancuso DM, Townsend MH, Mercante DE. Long-term follow-up of generalized anxiety disorder. *Compr Psychiatry* 1993;34:441–446
42. Noyes R Jr, Holt CS, Woodman CL. Natural course of anxiety disorders. In: Mavissakalian MR, Prien RF, eds. *Long-Term Treatments of Anxiety Disorders*. Washington, DC: American Psychiatric Publishing; 1996:1–48
43. Warshaw MG, Keller MB, Stout RL. Reliability and validity of the longitudinal interval follow-up evaluation for assessing outcome of anxiety disorders. *J Psychiatr Res* 1994;28:531–545
44. Yonkers KA, Massion AO, Warshaw MG, et al. Phenomenology and course of generalised anxiety disorder. *Br J Psychiatry* 1996;168:308–313
45. Yonkers KA, Dyck IR, Warshaw M, et al. Factors predicting the clinical course of generalised anxiety disorder. *Br J Psychiatry* 2000;176:544–549
46. Brawman-Mintzer O, Lydiard RB. Generalized anxiety disorder: issues in epidemiology. *J Clin Psychiatry* 1996;57(suppl 7):3–8
47. International Consortium of Psychiatric Epidemiology. Cross-national comparisons of the prevalences and correlates of mental disorders. WHO International Consortium in Psychiatric Epidemiology. *Bull World Health Organ* 2000;78:413–426
48. Noyes R Jr. Comorbidity in generalized anxiety disorder. *Psychiatr Clin North Am* 2001;24:41–55
49. Roy-Byrne PP, Katon W. Generalized anxiety disorder in primary care: the precursor/modifier pathway to increased health care utilization. *J Clin Psychiatry* 1997;58(suppl 3):34–38
50. Judd LL, Kessler RC, Paulus MP, et al. Comorbidity as a fundamental feature of generalized anxiety disorders: results from the National Comorbidity Study (NCS). *Acta Psychiatr Scand Suppl* 1998;393:6–11
51. Olfson M, Fireman B, Weissman MM, et al. Mental disorders and disability among patients in a primary care group practice. *Am J Psychiatry* 1997;154:1734–1740
52. Kessler RC. The prevalence of psychiatric comorbidity. In: Wetzler S, Sanderson WC, eds. *Treatment Strategies for Patients with Psychiatric Comorbidity*. New York, NY: John Wiley & Sons; 1997:23–48
53. Kessler RC. The epidemiology of pure and comorbid generalized anxiety disorder: a review and evaluation of recent research. *Acta Psychiatr Scand Suppl* 2000;406:7–13
54. Kessler RC, Andrade LH, Bijl RV, et al. The effects of comorbidity on the onset and persistence of generalized anxiety disorder in the ICPE surveys. *Psychol Med*. In press
55. Kessler RC, Greenberg PE, Mickelson KD, et al. The effects of chronic medical conditions on work loss and work cutback. *J Occup Environ Med* 2001;43(suppl 3):218–225
56. Kessler RC, Mickelson KD, Barber C, et al. The association between chronic medical conditions and work impairment. In: Rossi AS, ed. *Caring and Doing for Others: Social Responsibility in the Domains of Family, Work, and Community*. Chicago, Ill: University of Chicago Press; 2001
57. Weiller E, Bisslerbe JC, Maier W, et al. Prevalence and recognition of anxiety syndromes in five European primary care settings: a report from the WHO Study on Psychological Problems in General Health Care. *Br J Psychiatry* 1998;173(suppl 34):18–23
58. Wittchen HU, Carter RM, Pfister H, et al. Disabilities and quality of life in pure and comorbid generalized anxiety disorder and major depression in a national survey. *Int Clin Psychopharmacol* 2000;15:319–328
59. Andrews G, Henderson S, Hall W. Prevalence, comorbidity, disability and service utilisation: overview of the Australian National Mental Health Survey. *Br J Psychiatry* 2001;178:145–153
60. Kessler RC, Foster CL, Saunders WB, et al. Social consequences of psychiatric disorders. 1: educational attainment. *Am J Psychiatry* 1995;152:1026–1032
61. Kessler RC, Berglund PA, Foster CL, et al. Social consequences of psychiatric disorders. 2: teenage parenthood. *Am J Psychiatry* 1997;154:1405–1411
62. Kessler RC, Walters EE, Forthofer MS. The social consequences of psychiatric disorders. 3: probability of marital stability. *Am J Psychiatry* 1998;155:1092–1096
63. Woodward LJ, Fergusson DM. Life course outcomes of young people with anxiety disorders in adolescence. *J Am Acad Child Adolesc Psychiatry* 2001;40:1086–1093
64. Kennedy BL, Schwab JJ. Utilization of medical specialists by anxiety disorder patients. *Psychosomatics* 1997;38:109–112
65. Kessler RC, Olfson M, Berglund PA. Patterns and predictors of treatment contact after first onset of psychiatric disorders. *Am J Psychiatry* 1998;155:62–69
66. Olfson M, Kessler RC, Berglund PA, et al. Psychiatric disorder onset and first treatment contact in the United States and Ontario. *Am J Psychiatry* 1998;155:1415–1422
67. Ruscio AM, Borkovec TD, Ruscio J. A taxometric investigation of the latent structure of worry. *J Abnorm Psychol* 2001;110:413–422
68. Bienvenu OJ, Nestadt G, Eaton WW. Characterizing generalized anxiety: temporal and symptomatic thresholds. *J Nerv Ment Dis* 1998;186:51–56
69. Rickels K, Schweitzer E. The clinical presentation of generalized anxiety in primary-care settings: practical concepts of classification and management. *J Clin Psychiatry* 1997;58(11, suppl):4–10
70. Rickels K, Schweizer E. The spectrum of generalised anxiety in clinical practice: the role of short-term, intermittent treatment. *Br J Psychiatry Suppl* 1998;173:49–54