Public Health Perspectives on Generalized Anxiety Disorder

Murray B. Stein, M.D., M.P.H., F.R.C.P.C.

Generalized anxiety disorder (GAD) is a chronic condition characterized by worry and concomitant anxiety symptoms that cause extreme distress and/or interfere with function. The 12-month prevalence of GAD in the general population ranges in studies from approximately 2% to 5%, with the majority of cases occurring comorbid with major depression. GAD is particularly prevalent in certain special populations, such as older adults, in whom it is the most common anxiety disorder. In clinical and community studies, GAD emerges as a strong predictor of functional impairment, over and above that explained by major depression. These observations lead to the conclusion that current public health efforts focused on identification and treatment of major depression should be extended to include GAD and other anxiety disorders. *(J Clin Psychiatry 2004;65[suppl 13]:3–7)*

"Don't worry . . . be happy"

—Bobby McFerrin

Worry is a state of anxious apprehension and rumination that, by its very nature, is futile. Worrying about a child's health will not make the child feel better. Worrying about one's finances will not affect the bank balance. Worrying about meeting a deadline will not make time pass slower or put more hours in the day or days in the week. What worrying will do, however, is consume cognitive and emotional resources that could be put to better use. As the song suggests, worrying is an impediment to happiness. Yet, despite its pointless nature, worrying has become something of a national pastime, according to the prevalence rates reported for a disorder whose hallmark is worry, i.e., generalized anxiety disorder (GAD).

This article will provide some perspectives on epidemiologic and nosologic aspects of GAD, taking into consideration some complementary viewpoints on its comorbidity with other disorders. An additional focus will be on demonstrating the impact of GAD by reviewing evidence of its effects on functioning and health-related quality of life. Taken together, its prevalence and seriousness speak to the importance of GAD as a public health concern.

From the Department of Psychiatry, University of California San Diego.

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Corresponding author and reprints: Murray B. Stein, M.D., M.P.H., Department of Psychiatry, University of California San Diego (0985), 9500 Gilman Drive, La Jolla, CA 92093-0985 (e-mail: mstein@ucsd.edu).

EPIDEMIOLOGY OF GENERALIZED ANXIETY DISORDER

The very name chosen for this disorder, *generalized anxiety disorder*, has undoubtedly contributed to confusion about what the disorder is intended to characterize. The name conjures up images of an anxiety disorder that, rather than having specific symptoms, has generalized symptoms. Consequently, it is not unusual to see clinicians apply the GAD label to anyone with anxiety symptoms. Although this application is a tremendous time saver, it defeats the purpose of diagnostic criteria and is not appropriate. The *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) defines GAD as a chronic anxiety disorder (minimum 6 months duration) characterized by excessive, uncontrollable worry associated with fatigue, insomnia, muscle tension, poor concentration, and irritability.[1]

Prevalence

Studies using DSM-III-R or DSM-IV criteria find that GAD is a relatively common disorder in the general population, with 12-month prevalence rates ranging from 1.9% to 5.1%.[2] In the National Comorbidity Survey (NCS),[3] current prevalence of DSM-III-R GAD was 1.6%, but lifetime prevalence was considerably higher at 5.1% of the U.S. population aged 15 to 54 years. In a representative national survey[4] of 4181 adults aged 18 to 65 years in Germany, the 12-month prevalence rate of DSM-IV-defined GAD was 1.5%, with a total of 3.6% having either full or subsyndromal GAD symptoms. Most recently reported are data from the Australian National Survey of Mental Health and Well-Being (NSMH&WB),[5] a nationwide household survey of 10,641 Australian adults. Using DSM-IV criteria, prevalence was 2.8% for 1-month GAD and 3.6%

for 12-month GAD. Most studies find that GAD is more common in women and in older age groups.[6] The Longitudinal Aging Study Amsterdam,[7] which included a random sample of 3107 older adults (aged 55–85 years), found that the most common anxiety diagnosis was GAD, affecting 7.3% (6-month prevalence) of those surveyed.

Duration and Associated Symptoms

Symptoms of GAD may wax and wane over time, often in response to life stressors, but they rarely remit fully without treatment.[6] A naturalistic study[8] of 39 outpatients with GAD seen in the context of a clinical trial found that the majority of patients were still symptomatic 18 months later. In a study[9] of older adults in a clinical setting, it was found that the mean duration of GAD was 37.7 years. The various iterations of the DSM have wavered in their attempts to define the most appropriate symptom duration for a diagnosis of GAD. In one study, Bienvenu and colleagues[10] divided community subjects into 5 mutually exclusive symptom categories: (1) DSM-III-R GAD (i.e., 1-month duration), (2) 6 months of worry or anxiety with 6 associated symptoms, (3) 1 month of anxiety with 6 associated symptoms, (4) 1 month of anxiety without 6 associated symptoms, and (5) no anxiety. The authors investigated demographic and comorbidity profiles as external construct validators. The first 3 groups were similar with regard to these validators, but their profiles differed from those of subjects with fewer than 6 symptoms or no anxiety. Thus, requiring 6 symptoms produced a group with a particular epidemiologic profile, regardless of the duration of symptoms or the type of worries experienced by respondents. These data suggest that it is the co-occurrence of worry and multiple associated symptoms that seems to best define this syndrome and that duration of symptoms may matter less. It is unclear, however, if these provisions would apply equally well to a sample of patients seen in a clinical setting, where duration of illness may be important for separating adjustment disorders from GAD.

The requirement in DSM-IV that the worry be "uncontrollable" and occur "more days than not" has also come under fire. Ruscio et al.[11] have demonstrated that worry occurs along a continuum of severity, with no clear boundary between normal and abnormal worry. As such, worry as seen in GAD may be quantitatively rather than qualitatively different from normal functioning. Ruscio[12] also found that certain characteristics tended to distinguish high worriers with and without GAD; these factors included greater distress and impairment. Hoyer and colleagues[13] interviewed a representative sample of 2064 young women aged 18 to 25 years in Germany. They applied DSM-IV diagnostic criteria using a semistructured interview that was supplemented with questions about worry frequency, intensity, and uncontrollability. The authors found 37 women (1.8% point prevalence) who fulfilled DSM-IV criteria for GAD, whereas an additional 50 women (2.3%) had subthreshold GAD (i.e., met 3 of 4 DSM-IV GAD criteria). The authors found that both syndromal and subsyndromal GAD were associated with reduced levels of psychosocial functioning. The authors concluded that although the DSM-IV worry criteria are useful, attention should be paid to the potential importance of subthreshold generalized anxiety states in future studies.[13]

Another area in which the DSM has struggled is in deciding which symptoms should be included with worry to optimally define the syndrome. DSM-IV dropped autonomic symptoms of anxiety from the list of possible associated symptoms in GAD because they were infrequently found in GAD patients in psychiatric clinics.[14] The remaining symptoms (i.e., motor tension and vigilance/scanning), however, may not be characteristic of the kinds of symptoms experienced by patients in nonpsychiatric settings such as primary care.[15] These observations remind us that the diagnostic criteria for GAD and, indeed, our current classification system for mental disorders is a work in progress.[16,17] However, that realization should not deter us from using the extant diagnostic criteria to identify and treat patients who may benefit from intervention. It may be informative, however, to keep in mind alternative or complementary diagnostic systems that are currently being investigated.

Comorbidity

In a study of patients with principal anxiety and/or mood disorders in an anxiety disorders outpatient clinic, Brown et al. [18] found that current and lifetime prevalence of comorbid Axis I disorders were 57% and 81%, respectively. High comorbidity among anxiety and depressive disorders is a consistent finding in both clinical and community studies,[19–21] and GAD conforms to this general pattern. In a series of secondary analyses conducted in subjects in the NCS database, Judd and colleagues[22] found that approximately 80% of respondents with lifetime GAD also had a comorbid mood disorder during their lifetime. In both clinical and epidemiologic samples, GAD is highly comorbid with major depressive disorder (MDD),[3,23–26] raising questions about their diagnostic independence.[16] This topic will be revisited later in this article, when the burden of illness attributable to GAD is examined.

Zimmerman and Chelminski[27] examined the DSM-IV hierarchical requirement that forbids the diagnosis of GAD if it is present exclusively during the course of a mood disorder. Three hundred thirty-two psychiatric outpatients were interviewed, and investigators made diagnoses of DSM-IV GAD and "modified GAD" (which included all GAD criteria except for the hierarchical exclusion criterion). Analyses compared characteristics of 3 non-overlapping groups of patients with DSM-IV MDD: (1) those with coexisting DSM-IV GAD (i.e., symptoms were also evident outside of MDD episode[s]), (2) those with modified GAD, and (3) those with neither DSM-IV

nor modified GAD. Depressed patients with DSM-IV or modified GAD had higher levels of suicidal ideation, poorer social functioning, a greater level of pathologic worry, and more severe symptoms than those in the other disorder category. The 2 GAD groups (i.e., DSM-IV and modified GAD) did not differ from each other in these respects. The authors interpreted these data to mean that the DSM-IV hierarchical relationship between MDD and GAD is flawed, and they suggest that the exclusion criterion should be eliminated in future versions of the DSM. Implications of this change for research and clinical practice remain to be determined.

Another area of substantial comorbidity exists among anxiety and substance use disorders and, once again, GAD is no exception.[28–31] Most recently, results from the Australian NSMH&WB[28] showed that approximately 1 in 3 respondents with an alcohol use disorder (abuse or dependence) met criteria for at least 1 anxiety disorder during the previous 12 months; this was approximately triple the rate of persons without an alcohol use disorder. The odds of having GAD were increased 3-fold (odds ratio = 3.3, CI = 1.9 to 5.6) among persons with an alcohol use disorder compared with persons without an alcohol use disorder. These data should remind clinicians to ask about alcohol and other substance use in their patients with GAD.

Diagnosis in Special Populations

Children can also suffer from GAD. Pina and colleagues[32] administered a semistructured diagnostic interview to 111 youths (aged 6–17 years) and determined which symptoms contributed most to the DSM-IV diagnosis. They found that symptoms varied in the degree to which they contributed to diagnosis but that, in general, most were quite useful regardless of whether they were reported by the child/adolescent or parent.

GAD can also occur in older adults. Hopko and colleagues[33] reported that an abbreviated (8-item) version of the Penn State Worry Questionnaire,[34] a widely used measure to assess worry as part of GAD in younger adults, could be used for this purpose in late-life anxiety. This research group also conducted a study[35] wherein they examined the characteristics of GAD symptoms in older adults. In this study, they compared 30 older adults with diagnosable DSM-IV GAD with 19 older adults with subsyndromal GAD symptoms, which they term *minor GAD*, and 21 healthy control volunteers. Individuals with minor GAD had less severe impairment, had less difficulty controlling worry, and were less likely to endorse excessive worry more days than not compared with individuals with DSM-IV GAD. A discriminant function analysis, however, had difficulty distinguishing older adults with minor versus DSM-IV GAD, whereas the healthy volunteers were clearly set apart. These observations suggest that subsyndromal presentations of GAD are common in the elderly and echo the sentiments of Hoyer et al.[13] that clinicians should not ignore GAD-like syndromes simply because they fail to meet full DSM-IV criteria.

Although postpartum depression has been widely investigated, little work has been done to determine the prevalence of anxiety syndromes in the postpartum period. Wenzel and colleagues[36] completed an interview assessing anxiety and depression in a community-based sample of 68 women at 8 weeks postpartum. Three women (4.4%) met DSM-IV criteria for GAD, which was even more common in their sample than MDD, which occurred in 2 women (2.9%). More work needs to be done to confirm these findings and to consider the ramifications for the management of anxiety in women during the postpartum period.

DISABILITY AND QUALITY OF LIFE ASSOCIATED WITH GENERALIZED ANXIETY DISORDER

Given the extensive comorbidity between GAD and other mood and anxiety disorders, it has often been questioned to what extent the burden of disability associated with GAD can be considered a feature of that disorder as opposed to being attributable to the comorbid disorder(s). Several important studies have addressed this question making use of large primary care clinical or nationally representative community data sets.

An important issue is whether or not a diagnosis of GAD confers meaningful information over and above that conferred by a diagnosis of MDD alone. Specifically, if a diagnosis of GAD in someone with MDD adds nothing to prediction of course or outcome or to selection of treatment, then one might question the practical usefulness of the diagnosis of GAD. The literature in this regard has been mixed, with some primary care studies finding that GAD is associated with substantial disability[37] and others concluding that the associated disability is negligible.[38,39] As noted by other investigators,[40] relatively small sample sizes may have hampered the assessment of disability associated with GAD in the latter 2 studies.

More recently, the association between GAD and MDD has been examined from an epidemiologic perspective using nationally representative data. Kessler and colleagues[40] examined data from 2 large, representative U.S. national surveys (the NCS[41] and the Midlife Development in the United States Survey[42]) to investigate the associations between GAD, MDD, and functional impairment. Most respondents with GAD in a 12-month time period had comorbid MDD. To distill information about impairment associated with each disorder alone and both disorders together, the investigators compared groups of individuals with these particular characteristics. When comparing respondents with GAD but not MDD with those with MDD but not GAD and those with neither disorder, they found that both GAD and MDD were associated with comparable and independent functional impairment. Wittchen and col-

leagues[43] used a similar strategy to investigate the extent of work and social impairment in a nationally representative German sample, where they also found that GAD and MDD had comparable 12-month outcomes with regard to impairment. In both studies,[40,43] respondents with comorbid GAD and MDD had by far the highest levels of impairment. In the Australian NSMH&WB,[5] GAD was associated with significant disability even in the absence of comorbidity, though it was noted that comorbidity was associated with more profound functional impairment.

In a recent study, Offord and colleagues analyzed data from the Mental Health Supplement to the Ontario Health Survey,[44] a large Canadian epidemiologic survey that was contemporaneous, and nearly identical in design, to the NCS.[41] The Mental Health Supplement to the Ontario Health Survey included a series of questions about life satisfaction and well-being associated with psychiatric disorders in the community.[45,46] This dataset was used to examine relationships between GAD and MDD and health-related quality of life and impairment.[47] Consistent with prior epidemiologic surveys in other countries, GAD and MDD were found to be highly comorbid, from both cross-sectional and lifetime perspectives. Specifically, approximately one half of all cases of GAD were comorbid with MDD. Logistic regression methods examined impairment associated with GAD while adjusting for the presence of MDD (and vice versa) and other relevant covariates such as age and sex. These analyses found that, across a wide range of measures that included satisfaction with one's main activity (e.g., job, school) and overall sense of well-being, MDD and GAD were independently associated with poorer outcomes. On most measures (e.g., satisfaction with income or friendships), MDD was seen as more disabling, whereas on others (e.g., satisfaction with family life), the 2 disorders were associated with similar odds of being dissatisfied. For the most part, MDD could be considered "worse," i.e., more disabling, but the effect of GAD was still noteworthy and substantial. The directionality of these findings is in keeping with the observation that in mental health clinical settings, MDD accounts for more of the variance in impairment than GAD.[48] These data are complementary to those of the other community surveys[5,40,43] and go further by showing that the effects of GAD extend beyond demonstrable effects on work and social function to include pernicious effects on health-related quality of life.

SUMMARY

GAD as defined in DSM-IV, although highly comorbid on both cross-sectional and lifetime perspectives with other anxiety and mood disorders (most notoriously MDD), is emerging as an important predictor of disability and impaired life satisfaction. Numerous studies conducted over the past 5 years have documented the extent of disability associated with GAD in the community. Moreover, these studies have confirmed that even though GAD is often comorbid with depressive illness, it carries its own burden of disability that is largely independent of that of comorbid MDD. When these results are coupled with the fact that GAD is a chronic condition and information about its cost to the health care system and to society in general (as reviewed by Roy-Byrne and Wagner[49] in this supplement), it becomes clear that GAD should be considered a public health problem of considerable magnitude. It is hoped that future work will be conducted to determine optimal, cost-effective, population-based solutions to this problem.

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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