THE ECONOMIC BURDEN OF ANXIETY AND STRESS DISORDERS

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No society can afford to guarantee universal health insurance coverage for treatment of all illnesses for all of its citizens. The number of illnesses is simply too large and the costs of treatment too great for such a guarantee even in the most economically advantaged societies. Resource allocation rules are consequently needed (1). The most widely accepted of these rules emphasizes cost-effectiveness. According to this rule, medical interventions are appropriate only if their expected benefits clearly exceed the sum of their direct costs and their expected risks (2).

The difficulty in implementing this decision rule is that no obvious comparability exists between the single metric in which the costs of treatment are usually defined (i.e., dollars) and the many different metrics in which the benefits of treatment can be defined (e.g., physical pain, discomfort, psychological distress, and role impairment). To create transformations across these different metrics to allow for comparisons of costs and benefits on a single metric, a number of strategies have been developed, such as assessments of willingness to pay, time trade-off, standard gamble, and other utility or quasi-utility measures (3). In addition, a special interest has evolved in the indirect economic costs of illness and the benefits of treatment in terms of sickness absence and disability from work. The costs of these role impairments can be more easily assessed than the costs of other adverse effects of illness and represent the cost-benefit trade-off to purchasers of employer-sponsored health insurance plans (4).

The most ambitious effort to date to evaluate the costs of illness in terms of role impairments and disabilities is the World Health Organization (WHO) Global Burden of Disease (GBD) Study, an initiative designed to generate a rank ordering of the diseases that create the greatest societal burdens in terms of impairment and disability (5). The over-arching goal of GBD is to help health policy planners prioritize disorder-specific resource allocation decisions. GBD focuses on economic costs of illness using a metric known as the disability-adjusted life year (DALY) (6), a weighted composite that combines expected years of lost life with expected years of decreased functioning due to a particular disease (or constellation of comorbid diseases).

The first generation of GBD estimates suggest that mental disorders, as a group, are the most costly diseases in the world and that major depression, in particular, is the single most costly disease among people in the middle years of life in terms of overall DALYs (5). Although the GBD rated mood disorders as considerably more costly than anxiety or stress disorders, focused cost-of-illness studies carried out subsequent to the publication of these estimates strongly suggest that the GBD underestimated the costs of anxiety and stress disorders and that the true costs of anxiety disorders are actually quite comparable to the costs of mood disorders (7,8).

Three reasons for the underestimation of the costs of anxiety and stress disorders in the GBD are worthy of note. The evidence to support all three of them is reviewed in this chapter. First, the epidemiologic studies used in GBD underestimated the prevalences of anxiety disorders. Second, the estimated effects of specific diseases on functioning were based on the judgments of experts rather than on objective evaluations of actual impairments in representative samples of people with the diseases. These judgments underestimated the impairments due to anxiety disorders. Third, comorbidities were ignored in making GBD cost estimates. As shown below, a consideration of comorbidities is critical in assessing the costs of anxiety disorders.

This chapter reviews available evidence on the economic burdens of anxiety and stress disorders. By focusing on eight factors that lead to the high societal costs of these disorders, we present evidence on the three sources of GBD underestimation listed above. These eight factors are as follows. First, anxiety and stress disorders are among the most commonly occurring of all chronic diseases. Second, the prevalences of

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these disorders are increasing in recent cohorts in many countries. Third, these disorders have much earlier ages of onset than other commonly occurring chronic conditions. Fourth, anxiety and stress disorders are usually very chronic. Fifth, early-onset anxiety and stress disorders have a wide range of adverse effects on secondary outcomes, such as teen childbearing, marital stability, and educational attainment that have substantial economic implications. Sixth, these disorders are often associated with substantial impairments in role functioning. Seventh, anxiety and stress disorders are highly comorbid and usually temporally primary. Some of the disorders that are temporally secondary to anxiety and stress disorders, such as ulcers and substance abuse, have adverse economic effects that should be considered in part among the costs of anxiety and stress disorders. Eighth, despite the fact that effective treatments are available, only a minority of people with anxiety and stress disorders receives these treatments. Furthermore, those who receive these treatments usually do so only after many of the adverse effects of the disorders have occurred, making it very difficult to reverse the economic impacts of having had the disorders even with successful treatments. Based on all these factors, anxiety and stress disorders have to be considered among the most costly of all chronic physical and mental disorders.

PREVALENCES

A new generation of psychiatric epidemiologic surveys, which began with the Epidemiologic Catchment Area (ECA) Study in the early 1980s (9), has dramatically increased our knowledge about the general population prevalences and correlates of anxiety disorders. The ECA Study was the first psychiatric epidemiologic study to use a fully structured research diagnostic interview designed specifically for use by lay interviewers to operationalize the criteria of a wide range of mental disorders. This interview, known as the Diagnostic Interview Schedule (DIS) (10), was used throughout the 1980s and early 1990s to carry out parallel epidemiologic surveys in a number of countries (11,12). The DIS was also used as the basis for an elaborated interview developed by the WHO and known as the Composite International Diagnostic Interview (CIDI) (13). The CIDI was designed to generate diagnoses according to the definitions and criteria of both the International Classification of Diseases (ICD) and *Diagnostic and Statistical Manual of Mental Disorders* (DSM) systems. WHO auspices resulted in over a dozen large-scale, general-population CIDI surveys being carried out around the world over the past decade. Comparative analysis of these data has been facilitated by the creation of the WHO International Consortium in Psychiatric Epidemiology (ICPE) (14), which is currently coordinating national CIDI surveys in 25 countries around the world, with a combined sample size of over 150,000 respondents, as part of the WHO World Mental Health 2000 (WMH2000) Initiative (15).

The DIS and CIDI surveys show that anxiety and stress disorders are the most commonly occurring of all mental disorders. Clear illustration can be found in a recent report based on the results of six CIDI surveys carried out in Latin America, North America, and Europe (16). These surveys found that the lifetime prevalences of DSM third edition revised (III-R) anxiety disorders were as high as 25%, whereas prevalences in the year before the survey were as high as 17%. These prevalences were higher than those of any other class of mental disorders in the vast majority of the surveys. (The exceptions were a survey of adolescents in Germany and of residents of a large catchment area in Mexico City. In both of these surveys, substance use disorders were more common than anxiety disorders in the 12 months before the interview.)

It was noted above that the epidemiologic data available to the GBD researchers, which came from the DIS surveys carried out in the 1980s, underestimated the prevalence of anxiety and stress disorders. Three of the most prevalent and seriously impairing anxiety disorders were involved in this underestimation: generalized anxiety disorder (GAD), social phobia, and posttraumatic stress disorder (PTSD). The reasons for the underestimations differ from one of these disorders to the next. In the case of GAD, prevalence was underestimated in the early DIS surveys due to the fact that the excessively unrealistic criterion in the DSM-III was operationalized by requiring that respondents endorse a statement that they worried about things that were not really serious or about things that were not likely to happen. This requirement is overly restrictive in two ways. First, there is no requirement in DSM that people with GAD have insight into their worries being excessive or unrealistic. Although they must be aware that they worry more than other people do, they can perceive others as worrying too little rather than themselves as worrying too much. Second, even in the presence of a recognition that their worrying is excessive, there is no requirement in DSM that the worries of people with GAD must be exclusively focused on things that are not important or unlikely to happen. Indeed, the heterogeneous worries that are characteristic of most people with GAD (e.g., excessive concerns about job stability, how the children are going to turn out, neighborhood safety, global warming, etc.) often focus on serious matters that have nontrivial probabilities of occurring.

The restrictive assessment in the DIS led to the estimate that only about 3% of the population meet criteria for GAD at any time in their lives (17). Early CIDI surveys followed this same method of assessment and yielded similar prevalence estimates (18,19). Subsequent CIDI surveys expanded the assessment of excessive worry in GAD by asking respondents if there was ever a time in their lives when they were worriers or when they worried a lot more than most other people in their same situation, without requiring that

the worry be exclusively about things that are not serious or not likely to happen. Prevalence estimates were found to be considerably higher when this modification was introduced (20).

In addition, these new studies investigated the implications of the requirements in the DSM-IV and ICD-10 that the worry in GAD persists for a minimum of 6 months and found that this requirement might be too restrictive. In particular, many people with chronic excessive worry report having fairly short episodes, each of which lasts for several weeks or months, that continue in a chronic intermittent course for many years. Such individuals are currently excluded from a diagnosis of GAD and, because of their high comorbidity with depression, are classified as being depressed even though their most prominent symptoms are often associated with anxiety rather than depression. The new WHO WMH2000 Initiative is investigating this matter in some detail in an effort to evaluate whether the classification rules for GAD or mixed anxiety-depression should be modified to take these cases into consideration.

In the case of social phobia, the underestimation in the early DIS surveys was due to the fact that all phobias were assessed in a single question that presented respondents with a long checklist of feared situations and asked them if they ever had unreasonably strong fears of these situations. In addition to being mixed in with a number of specific fears, only five social phobic situations, all involving performance fears, were included in the ECA list.

This method of assessment led to the estimate that only 2.7% of the population meet criteria for social phobia at any time in their lives (21). Subsequent surveys that used the CIDI corrected this problem by screening for social phobia with a separate, longer list of social fears (both interactional and performance). These later surveys consistently found social phobia to be much higher than in the DIS surveys, with lifetime prevalences as high as 13% (18) and current prevalences as high as 8% (22).

Posttraumatic stress disorder was also wildly underestimated in the early DIS surveys. This seems to have been a result of including only a single extremely long and complex screening question for PTSD in the first version of the DIS. This question began with a statement that many people live through events that are outside the range of usual human experience, such as combat in a war or sexual assault, and that people who experience these events often have bad emotional reactions such as nightmares, flashbacks, and changes in mood. Respondents were then asked if they ever had such an event that caused such reactions and, if so, to tell the interviewer what this event was. Subsequent debriefing showed that this question was too complex for many respondents, that the absence of a detailed event list interfered with effective memory search, and that the requirement that the respondent describe the event out loud rather than give a yes or no response to event-specific questions led to underreporting of embarrassing events (23).

Assessments of PTSD in epidemiologic surveys that used the DIS led to the estimate that only about 1% of the United States population meet criteria for this disorder at any time in their life (24–26). Subsequent surveys that used the CIDI modified the assessment of PTSD by including a detailed traumatic event checklist and by asking respondents to give separate yes or no reports for whether each of these events ever occurred to them. In some CIDI surveys, a visual checklist was used that aimed at making it easier for respondents to report embarrassing events (e.g., "Did event number five on the list ever occur to you?" rather than "Were you ever raped?"). CIDI PTSD symptom assessment proceeded very much along the same lines as the DIS after documenting that trauma exposure had occurred. Yet the prevalence estimates obtained in the CIDI surveys were dramatically higher than in the DIS surveys, with lifetime prevalences as high as 12.2% (23,27).

It should also be noted that psychiatric epidemiologic surveys have not, up to now, attempted to assess either DSM acute stress disorder (a short-term disorder that occurs in reaction to traumatic stress) or adjustment disorder (a disorder that occurs in reaction to nontraumatic stress). This is important because epidemiologic surveys that include assessments of current nonspecific psychological distress typically find that a high proportion of the respondents who report clinically significant current distress in the anxiety-mood spectrum do not meet criteria for any of the anxiety or mood disorders typically assessed in these surveys (which usually include GAD, panic disorder, phobia, PTSD, obsessive-compulsive disorder, major depression, dysthymia, and mania). Given the extremely high prevalences of exposure to stressful events found in surveys of stress exposure (28), it is plausible to think that many of these people have a diagnosis of either acute stress disorder or adjustment disorder. The new WHO WMH2000 surveys mentioned earlier in this chapter are investigating this possibility by evaluating the link between stress and clinically significant nonspecific psychological distress among respondents who do not meet criteria for other anxiety or mood disorders.

Taken together, these results suggest that the combined prevalences of all anxiety and stress disorders make these among the most commonly occurring classes of seriously impairing chronic conditions. A rough comparison is provided by the recently completed Midlife Development in the U.S. (MIDUS) survey carried out by the John D. and Catherine T. MacArthur Foundation. In this survey, parallel assessments were made of commonly occurring physical and mental disorders, along with assessments of the effects of these disorders on day-to-day functioning (29). As in most other health surveys of chronic physical conditions, of which a great many exist (e.g., 30,31), the significantly impairing physical disorders with the highest reported prevalences in the year before interview were back problems (20.3%), arthritis (19.4%), hypertension (18.2%), and seasonal allergies (15.7%). However, past health surveys of

chronic physical conditions have seldom assessed emotional disorders along with these physical disorders. In doing so, the MIDUS survey found that 16.4% of respondents reported an anxiety or stress disorder exclusive of either major or minor depression, and that an additional 14.1% of respondents reported major or minor depression. These findings make anxiety-stress the fourth most commonly occurring impairing class of chronic disorders in the general population and major or minor depression the sixth most commonly occurring class of such disorders.

COHORT EFFECTS

In addition to anxiety and stress disorders having great importance because they are very common, they are also becoming increasingly prevalent over time. An illustration of this finding is presented in Table 67.1, taken from ICPE surveys carried out in six countries (16). These results are based on synthetic cohort analyses using retrospective age-at-onset reports to evaluate intercohort differences in lifetime risk of anxiety disorders over a period of four decades. The data are clear in showing that the relative odds of having an anxiety disorder have steadily increased over this period in all six countries.

More detailed analyses of these and other data show that the increased prevalences of anxiety disorders are more pronounced than the increased prevalences of other mental disorders and that the apparent cohort effects for some other disorders, such as major depression, are largely due to increases in secondary disorders associated with primary anxiety (32). Furthermore, the increasing prevalences within the anxiety disorders have been found to be especially pronounced for GAD, generalized social phobia, and PTSD.

TABLE 67.1. THE EFFECTS (ODDS RATIOS) OF COHORT IN PREDICTING LIFETIME ANXIETY DISORDERS IN SIX COUNTRIES[a]

	Age Group				
	18–24	25–34	35–44	45–54	χ^2_3
Brazil	3.3*	3.1*	1.8*	1.0	64.4*
Canada	1.9*	1.7*	1.4*	1.0	20.7*
Mexico	2.1	2.0	2.0	1.0	2.3
Netherlands	2.2*	1.8*	1.5*	1.0	88.4*
Turkey	1.8*	1.7*	1.3	1.0	18.0*
United States	1.8*	1.4	1.1	1.0	27.9*

[a]Results are based on discrete-time survival analysis.
*Significant at the .05 level, two-sided test.
From WHO International Consortium of Psychiatric Epidemiology: cross-national comparisons of the prevalences and correlates of mental disorders: an ICPE study. *Bull WHO* 2000;78:420, with permission.
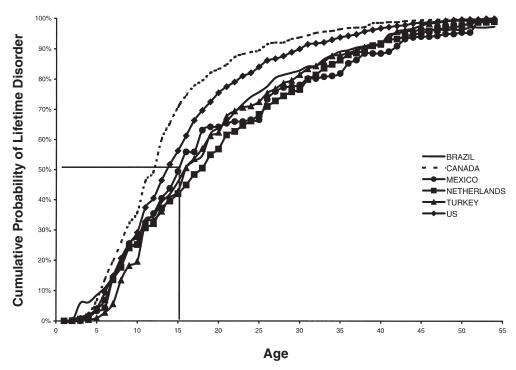
Increases for panic, specific phobia, agoraphobia, and obsessive-compulsive disorder, in comparison, have been more modest. Although these studies have not investigated either acute stress disorder or adjustment disorder, separate evidence of secular increases in exposure to traumatic stress is consistent with the likelihood that the prevalences of these disorders have also been on the rise (33).

AGE AT ONSET

The discussion up to now has not clearly distinguished between lifetime and recent prevalences. This is an important distinction because the societal burden of a disorder is largely associated with its prevalence at a point in time. The latter, in turn, is a complex function of lifetime prevalence, age at onset, and chronicity. The comparatively high recent prevalence of anxiety-stress disorders found in the MIDUS survey indicates that the combined effects of these three components are strong. This is true, in part, because anxiety and stress disorders occur to a high proportion of the population at some point in the course of life. It is also true because these disorders have comparatively early ages at onset and high rates of chronicity. We focus first on age at onset.

Retrospective reports about age at onset are routinely collected in epidemiologic surveys and used to estimate synthetic onset distributions. Figure 67.1 presents Kaplan-Meier curves that show these onset distributions for any anxiety disorders in six countries the ICPE surveyed (16). The median age at onset of anxiety disorders in these surveys is less than 15 years of age. The only commonly occurring chronic physical disorder that has a similar age-at-onset distribution is hay fever. All other commonly occurring chronic physical disorders that have been shown to have an effect on role functioning have median ages at onset that occur much later, in some cases decades later, than anxiety disorders. Other mental disorders, including depression, substance use disorders, oppositional-defiant disorder, conduct disorder, and attention-deficit hyperactivity disorder, also have comparatively early ages at onset, although anxiety disorders are the temporally primary disorders in the vast majority of people with a lifetime history of any mental disorder (34). No information is available, in comparison, on age at onset of acute stress disorders or adjustment disorders.

CHRONICITY

Although psychiatric epidemiologic surveys typically are cross-sectional, making it impossible to track illness course, indirect assessments of chronicity in these surveys have been carried out by comparing the ratios of current prevalence

FIGURE 67.1. Age-at-onset distributions for any anxiety disorders in six countries. (Modified from WHO ICPE. Cross-national comparisons of the prevalences and correlates of mental disorders: an ICPE study. *Bull WHO* 2000;78:418, with permission.)

to lifetime prevalence in subsamples of respondents with specific lifetime mental disorders. Results clearly suggest that anxiety disorders are the most chronic of all mental disorders (35). This indirect evidence is consistent with the results of longitudinal studies carried out in clinical samples, which uniformly show that anxiety disorders are typically very chronic (36–38). It is noteworthy that this high chronicity is not greater than that found among a number of impairing physical disorders, such as arthritis, asthma, and diabetes. However, the combined occurrence of high lifetime prevalence with early age at onset and high chronicity makes anxiety disorders unique. The one chronic physical disorder with comparable lifetime prevalence and early onset, hay fever, is active for only a few weeks each year. No systematic data exist on the chronicity of adjustment disorders, although epidemiologic data showing that PTSD is often a very persistent disorder (23,39) are consistent with the possibility that the same may be true for adjustment disorders.

ADVERSE EFFECTS ON SECONDARY OUTCOMES

Virtually all cost-of-illness studies focus on the effects of prevalent disorders on current role functioning, taking cur-

rent roles as givens. The question implicitly addressed by these studies is whether it is in the financial interests of employers to invest in employee health care. Would the increased direct costs of treatment be offset by decreased indirect costs in such things as sickness absence, poor work performance, and accidents? This important question is discussed below. However, even when the focus is on narrow financial costs, the preceding is not the only question of importance in evaluating the societal costs of illness. Equally, if not more, important from a societal perspective is the question of whether the human capital potential of the individual is adversely affected by illness. Specifically, what difference does the existence of a particular chronic condition make to the individual's lifetime profile of productivity?

There is good evidence that anxiety disorders have long-term effects of this sort that are not captured in analyses of current role functioning. Both vital statistics (see Table 292A, Trend C in ref. 40) and prospective epidemiologic surveys (41) show that anxiety is associated with elevated risk of early death. Epidemiologic data also show that anxiety is associated with elevated risk of subsequent unemployment (42,43).

Clinical experience also suggests that anxiety is associated with more subtle decrements in role performance. It is common for patients with chronic GAD or PTSD, for example,

to work at low-paying jobs because they are unable to cope with the stresses of higher paying jobs. This would be considered a cost of illness from the societal perspective, but not from the perspective of the employer. Very little scientific evidence exists regarding opportunity costs of this sort. The most sustained examination of these costs was carried out in a series of reports from the National Comorbidity Survey (NCS) in which retrospective reports about the ages at onset of individual mental disorders were used to define time-varying predictors of subsequent transitions in educational attainment (44), teen childbearing (45), marital timing and stability (46), and earnings (42,43). The results clearly show that mental disorders, in general, and anxiety disorders, in particular, are associated with significantly elevated risks of several different life course events that have important adverse financial implications. In terms of standardized (for sociodemographics) odds ratios, NCS respondents with some early-onset anxiety disorders had 40% elevated odds of high school and college failure, 30% elevated odds of teenage childbearing, 60% elevated odds of marital instability, and 150% elevated odds of current unemployment at the time of interview.

It is important to recognize that this constellation of adverse individual life course consequences—especially school failure coupled with teen childbearing and marital instability—makes up the core components of welfare dependency. The costs of public assistance to single mothers with dependent children are paid by all taxpayers rather than by the welfare recipients themselves. For this reason, the component of welfare dependency costs explained by early-onset anxiety disorders should be considered a societal cost of anxiety. A number of innovative welfare-to-work programs are currently being carried out in response to welfare reform legislation in the United States (e.g., 47,48). Interestingly, early reports on these programs suggest that their success hinges on the mental health of welfare recipients (49).

EFFECTS ON CURRENT ROLE FUNCTIONING

As noted in the previous subsection, a number of cost-of-illness studies have evaluated the effects of chronic conditions on work role functioning. Most of these studies focus on physical disorders (e.g., 31). Most of those concerned with mental disorders focus on depression (e.g., 50). A small number of recent studies examined the effects of anxiety disorders on work functioning and found that these effects are quite substantial. These findings are an important element in the argument that anxiety disorders are among the most costly of all chronic conditions.

One of these studies, based on the NCS, examined the effects of individual mental disorders on work loss (missing a full day of work) and work cutback (either missing part of a day or working less efficiently than usual) during the month prior to the interview (51). Each of the six anxiety disorders evaluated in that study (GAD, panic disorder, specific phobia, social phobia, agoraphobia, and PTSD) had significant effects on work-cutback days, from a high of 4.9 days per month associated with PTSD to a low of 1.1 associated with social phobia. None of the six was significantly associated with work-loss days, implying that anxiety influences work largely by affecting the quality of performance on days at work rather than by reducing the amount of time spent at work.

The MIDUS survey yielded information that is even more interesting because it assessed both mental and physical disorders. Gross bivariate analyses showed that two mental disorders, both anxiety disorders, were among the top five of all chronic conditions in terms of average per capita number of past month work impairment days. These top five included GAD (6.0 work impairment days per month), thyroid disease (5.8 days), tuberculosis (5.4 days), varicose veins (5.4 days), and panic disorder (5.3 days). Furthermore, multivariate analyses controlling for age, gender, and other sociodemographic factors found that the same two anxiety disorders were among the top six in terms of unique effects on work impairment (29). Calculating the salary-equivalent magnitude of these effects, using self-reported salaries and partialing out the effects of other comorbid mental and physical disorders, led to the estimate that the excess absenteeism and lost productivity directly associated with anxiety disorders is approximately $4.1 billion per year in the United States (8).

PSYCHIATRIC COMORBIDITY

A number of studies in both treatment samples (52) and general population samples (35) document high rates of psychiatric comorbidity among people with anxiety disorders. Illustrative results from the NCS are reported in Table 67.2. Shown here are odds ratios between anxiety disorders and other mental disorders both for lifetime comorbidities and for comorbidities of disorders that were active in the 6 months prior to the interview. As the latter odds ratios are generally larger than the former, there must be comorbidities between the persistence of anxiety disorders and the persistence of other disorders.

Several different possible explanations exist for these comorbidities. One is that prior history of other mental disorders might be associated, either as a risk factor or as a marker, with risk of the subsequent onset and persistence of anxiety disorders. The other is that anxiety disorders might be associated with the subsequent onset and persistence of other mental disorders. As briefly mentioned above, epidemiologic studies have found that the latter possibility is more consistent with the data. Comorbid anxiety disor-

TABLE 67.2. COMORBIDITIES (ODDS RATIOS) BETWEEN DSM-III-R ANXIETY DISORDERS AND OTHER MENTAL DISORDERS ASSESSED IN THE NATIONAL COMORBIDITY SURVEY

	Panic Disorder	Phobias	GAD	PTSD
Lifetime comorbidities				
Major depression	6.6	4.1	9.4	5.2
Dysthymia	4.8	3.0	12.5	4.9
Mania	10.4	7.9	9.6	6.2
Alcohol abuse/dependence	1.6	1.7	2.0	1.7
Drug abuse/dependence	3.0	2.2	2.9	3.2
Nonaffective psychosis	20.1	4.7	15.0	9.4
Six-month comorbidities				
Major depression	14.4	6.4	17.8	7.1
Dysthymia	12.2	4.4	21.5	7.4
Mania	15.8	13.4	10.4	9.4
Alcohol abuse/dependence	1.4	2.3	2.7	2.2
Drug abuse/dependence	3.9	3.9	5.0	2.9
Nonaffective psychosis[a]	—	—	—	—

All values on table are significant at the .05 level, two-sided test.
DSM-III-R, *Diagnostic and Statistical Manual of Mental Disorders*, third edition–revised; GAD, generalized anxiety disorder; PTSD, posttraumatic stress disorder.
[a]Diagnostic hierarchy rules were suppressed in defining the disorders. Six-month nonaffective psychosis (NAP) was too rare to calculate odds-ratios with any of the anxiety disorders.
From Tsuang MT, Tohen M, Zahner GEP, eds. *Textbook in psychiatric epidemiology*. New York: Wiley, 1995:181, 183, with permission.

ders are usually temporally primary to other comorbid mental disorders (34). In addition, survival analyses show that temporally primary anxiety disorders are powerful predictors of the subsequent onset and course of other mental disorders (35). In addition, panic disorder (53) and PTSD (54) are powerful predictors of suicidal behaviors.

It is not clear from these results that anxiety disorders are causal. Another possibility is that anxiety disorders are early outcomes of other causal factors, either environmental or genetic, that cause both anxiety disorders and the other mental disorders with which anxiety disorders are comorbid. To the extent that anxiety disorders are causal, the adverse effects of mental disorders that are secondary to anxiety disorders should be counted among the adverse consequences of anxiety disorders. A good case in point is secondary substance use disorders. Epidemiologic data show that early-onset anxiety disorders are significant predictors of subsequent substance use disorders, most likely mediated by self-medication (55). If these associations are causal, simulations suggest that the early intervention and successful treatment of anxiety disorders would prevent as many as one-fourth of all substance use disorders in the U.S. (56). The component of the costs of substance use disorders due to prior anxiety disorders, therefore, should be counted among the costs of anxiety in a comprehensive evaluation.

Whether anxiety disorders are causal and to what extent is an especially important issue in the case of depression, as many comparative cost-of-illness studies, including the

WHO GBD study, suggest that depression is the most costly of all mental disorders (5). Yet epidemiologic data show that close to half of all cases of depression are secondary to one or more preexisting anxiety disorders (57). This priority of anxiety over depression is never taken into consideration in evaluating the costs of depression. Indeed, in those few instances where anxiety-depression comorbidity is considered, diagnostic hierarchy rules typically specify that the depression should be considered primary even though epidemiologic evidence consistently shows that anxiety is usually temporally primary.

The rationale for this hierarchy of depression over anxiety is usually that the impairments associated with such cases is thought to be due to the depression rather than to the anxiety (58), but available evidence argues against this claim. A good case in point involves comorbidity between GAD and depression. The results in Table 67.3, taken from two U.S. national surveys, the NCS and the MIDUS, show that GAD without major depression is as important as major depression without GAD in leading to impairments in role functioning (20). Further analysis of these data showed that impairment is considerably higher among people with comorbid GAD and major depression than those with either GAD alone or major depression alone. Coupling the fact that GAD is temporally primary in the majority of these cases with the fact that GAD without major depression is associated with impairments equal to those of major depres-

TABLE 67.3. THE EFFECTS (ODDS RATIOS) OF 12-MONTH GENERALIZED ANXIETY DISORDER (GAD) WITHOUT MAJOR DEPRESSION (MD) AND MAJOR DEPRESSION WITHOUT GAD IN PREDICTING IMPAIRMENTS IN TWO U.S. NATIONAL SURVEYS, CONTROLLING FOR SOCIODEMOGRAPHICS AND OTHER 12-MONTH DSM-III-R DISORDERS[a]

	GAD Without Major Depression (MD)		Major Depression (MD) Without GAD		GAD Without MD vs. MD Without GAD	
	Survey 1	Survey 2	Survey 1	Survey 2	Survey 1	Survey 2
Fair/poor perceived mental health	6.0*	4.8*	3.3*	5.2*	1.6	0.8
High work impairment	3.5	3.5	3.5*	8.5*	0.9	0.5
High social impairment	2.5*	1.2	2.0*	1.6*	1.5	1.0

[a]The two surveys indicated here are the National Comorbidity Survey (Survey 1) (59) and the Midlife Development in the U.S. Survey (Survey 2) (19). Results are based on separate regression equations evaluating the effect of either GAD or MD in predicting one of the impairment measures in one of the samples controlling for sociodemographic variables (age, gender, education, race-ethnicity, employment status, marital status, and urbanicity) and other 12-month DSM-III-R disorders. Models in the first two columns evaluate the effect of 12-month GAD on the subsample of respondents who did not have 12-month major depression. Models in the middle two columns evaluate the effect of 12-month major depression on the subsample of respondents who did not have 12-month GAD. Models in the last two columns evaluate the relative impairments of GAD without MD versus MD without GAD in analyses that are confined to respondents in those two subsamples.
*Significant at the .05 level, two-sided test.
From Kessler RC, DuPont RL, Berglund P, et al. Impairment in pure and comorbid generalized anxiety disorder and major depression in two national surveys. *American Journal of Psychiatry* 1999; 156:1915–1923, with permission.

sion without GAD, argues that this interactive effect is due at least as much to GAD as to major depression.

PHYSICAL COMORBIDITY

Although it has not been as extensively studied, evidence from clinical samples suggests that anxiety disorders have significant comorbidities with certain chronic physical disorders (60,61). Table 67.4 presents nationally representative general

The results are odds ratios for the relationships between the 12-month prevalences of the DSM-III-R anxiety disorders assessed in the NCS and selected physical disorders assessed in the NCS chronic conditions checklist. As shown in the table, all but one of the odds ratios are greater than 1.0, indicating a positive relationship, and half are statistically significant at the .05 level.

The NCS did not obtain information about age at onset for these physical disorders, making it impossible to examine whether anxiety disorders are temporally primary. In some cases, such as the strong association of some anxiety disor-

TABLE 67.4. COMORBIDITIES (ODDS RATIOS) BETWEEN 12-MONTH PREVALENCES OF DSM-III-R ANXIETY DISORDERS AND CHRONIC PHYSICAL DISORDERS IN THE NATIONAL COMORBIDITY SURVEY

	GAD	Panic Disorder	Simple Phobia	Social Phobia	Agoraphobia	PTSD
Arthritis	1.7	2.1*	1.4	1.2	1.5	2.0*
Asthma	1.9	2.1*	2.0*	1.4	1.2	1.7*
Hypertension	1.5	2.2*	1.5*	1.0	2.2*	1.6
Kidney/liver disease	2.0	1.4	3.5*	1.2	2.3	1.9
Ulcer	3.1*	2.7*	2.7*	2.7*	2.9*	2.0*

*Significant at the .05 level, two-sided test.

ders with ulcers, the most plausible interpretation is that anxiety had a causal impact on the subsequent onset of the physical condition. In other cases, it is equally plausible that the physical condition helped promote the subsequent onset of anxiety. It is also possible that bidirectional causal influences were at work or that common causes led to both conditions. The eventual resolution of this uncertainty is important for an evaluation of the costs of anxiety disorders, as both the direct treatment costs and the indirect costs of physical disorders that are partly caused by anxiety should be included in evaluating the overall societal costs of anxiety.

Comorbidities of anxiety with physical disorders are also important because of evidence that anxiety disorders reduce the quality of life of patients with physical disorders (62) and complicate the expression and course of physical disease (63). The most plausible explanation for these findings is that anxiety heightens sensitivity about both physical signs and symptoms and adequacy of treatment. This possibility is consistent with the finding that adjunctive treatments for comorbid anxiety often increase adherence to physical disorder treatment regimens (64).

MENTAL HEALTH TREATMENT

Effective psychological (65) and pharmacologic (66) therapies exist for the treatment of most anxiety disorders. The indirect costs of anxiety disorders would consequently be expected to decline if a high proportion of people with these disorders sought treatment. However, a substantial part of the adverse effects of anxiety disorders are associated with secondary effects that occur early in life (e.g., teen childbear-

ing, school failure), so it is important that treatment occur early in the course of the anxiety disorder. As anxiety disorders have early ages of onset, initial treatment must occur during childhood or adolescence to be maximally effective in preventing adverse effects.

We are aware of only two epidemiologic studies that investigated speed of initial treatment contact after first onset of anxiety disorders (67,68). These studies considered three anxiety disorders: GAD, panic disorder, and phobias. Both studies found that only a small proportion of people with childhood-onset or adolescent-onset anxiety disorders seek treatment prior to adulthood. Median delays between first onset and initial treatment contact were found to be more than a decade for some anxiety disorders. Furthermore, delays were found to be inversely related to age at onset.

Because of these delays, only a minority of people with active anxiety disorders receives treatment in a given year. This is shown clearly in Table 67.5, which presents nationally representative U.S. data from the NCS on seeking professional help for DSM-III-R anxiety disorders during the 12 months prior to the survey. Only about one out of every four people with an anxiety disorder sought any type of treatment and only 13.3% received any type of mental health specialty treatment during this year.

INAPPROPRIATE USE OF GENERAL MEDICAL SERVICES

Although anxiety disorders typically are not treated, it is a great irony that people with anxiety disorders are often high

TABLE 67.5. 12-MONTH PREVALENCE OF PROFESSIONAL HELP-SEEKING IN SEPARATE SERVICE SECTORS IN THE NATIONAL COMORBIDITY SURVEY, BY 12-MONTH DSM-III-R ANXIETY DISORDER

| | Help-Seeking in Health Care Sectors[a] | | | | | | Help-Seeking in Other Sectors[a] | | | | | |
| | General Medical | | Specialty Mental Disorders | | Any | | Human Services | | Self-Help | | Any Help-Seeking[a] | |
Disorder	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)	%	(SE)
Generalized anxiety disorder	18.6	(3.8)	19.8	(3.5)	31.8	(4.8)	10.8	(2.1)	11.0	(3.0)	38.7	(4.3)
Panic disorder	21.5	(5.1)	24.3	(4.4)	35.2	(5.6)	21.0	(4.2)	12.5	(4.1)	46.4	(6.6)
Simple phobia	8.5	(1.4)	12.5	(1.5)	16.4	(1.7)	10.6	(1.8)	8.1	(1.3)	25.7	(2.3)
Social phobia	5.9	(0.9)	11.3	(1.7)	15.3	(1.9)	8.0	(1.3)	7.0	(1.5)	23.0	(2.2)
Agoraphobia	13.6	(3.6)	15.7	(3.2)	24.9	(4.7)	12.5	(3.1)	9.2	(2.9)	33.2	(5.0)
Posttraumatic stress disorder	12.5	(2.4)	22.3	(3.4)	28.2	(3.6)	16.3	(2.3)	11.8	(2.9)	38.3	(4.2)
Any	9.0	(1.3)	13.3	(1.4)	18.7	(1.7)	9.6	(0.9)	8.2	(1.0)	26.5	(2.0)

SE, standard error.
[a]Prevalence estimates are percentaged by rows. For example, in the first row of numbers, 18.6% is the percent of people with generalized anxiety disorder who used general medical services, not the percent of people using general medical services who carried a diagnosis of generalized anxiety disorder.
American Journal of Psychiatry 1999;156:117, with permission.

utilizers of primary care services. Indeed, people with untreated anxiety disorders make up a large proportion of the people who overuse primary care for only vaguely defined physical complaints (69,70). A recent anxiety disorders cost-of-illness study estimated that unnecessary medical care costs represented the largest single component of the cost of anxiety disorders in the U.S., equal to $23 billion per year (8). There is good reason to believe that aggressive screening and outreach efforts in primary care could detect these people with untreated anxiety, channel them into appropriate treatment, and possibly have a major offset effect in reducing unnecessary primary care costs. Interventions to evaluate the magnitude of this offset effect are currently under way.

OVERALL COSTS

There have been two recent attempts to estimate the total annual cost of anxiety disorders in the U.S. The first, carried out by DuPont et al. (7) in 1996, estimated that the annual cost of anxiety disorders is $47 billion, whereas the second, carried out by Greenberg et al. (8) in 1999, estimated that this cost is $42 billion. These estimates are quite comparable to the annual cost of depression, which has been estimated to be between $44 billion (71) and $53 billion (72). The rough equivalence to the cost of depression is important because, as noted in the introduction, depression is generally considered the most costly of all physical or mental disorders among people in the early to middle years of life (5).

The true societal costs of anxiety disorders, however, are actually a great deal larger than these estimates suggest, as the estimates were based only on a limited set of cost components. The components included direct psychiatric treatment costs, unnecessary medical treatment costs, work performance costs in terms of sickness absence and work-cutback days, and mortality costs (evaluated as lost earnings potential). The major excluded costs were long-term opportunity costs (i.e., excess unemployment and underemployment) and costs associated with comorbidity. The first of these two excluded costs is likely to be in excess of $2,000 per year for each person with a lifetime history of anxiety disorder (42), which is equivalent to an annual cost of more than $100 billion in the total U.S. population. The second of the excluded costs is impossible to calculate with currently available data, but would have to include substantial components of the costs conventionally attributed to depression, alcohol, and drug abuse, and the many other mental and physical disorders with lifetime prevalences and courses that are influenced by the prior existence of anxiety disorders.

DISCUSSION

Anxiety disorders are unique among all chronic conditions, both physical and mental, in having a combination of very high prevalence, early age at onset, high chronicity, and substantial role impairment. Although our knowledge about the comparative costs of different illnesses is too primitive to make precise comparisons, this conjunction of factors arguably makes anxiety disorders one of the most costly classes of illness in existence. Increased treatment is the key to reducing these costs. Although an increase in treatment will add to direct costs, the fact that available treatments are effective and that the adverse effects of anxiety are chronic means that the costs of effective treatment can be amortized over many years.

The fact that most anxiety disorders have childhood or adolescent onsets means that early outreach and treatment could be carried out in collaboration with schools. Unfortunately, as most people with anxiety delay initial contact with the treatment system for many years and usually present for treatment only after the onset of secondary comorbid disorders, little is known about the long-term effects of early treatment of pure childhood and adolescent anxiety disorders. Demonstration projects and long-term follow-up studies are needed to evaluate these effects and to target opportunities for incremental cost-effectiveness associated with refinements in diagnosis and treatment. Although the outcomes of such studies are uncertain, it is difficult to think of another disorder where an investment in early intervention has as great a potential for long-term societal benefits.

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