Functioning and Disability Levels in Primary Care Outpatients with One or More Anxiety Disorders (PM #8021)

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Abstract

Background—Anxiety disorders are the most prevalent mental health disorders and are associated with substantial disability and reduced well-being. It is unknown whether the relative impact of different anxiety disorders is due to the anxiety disorder itself or to the co-occurrence with other anxiety disorders. This study compared the functional impact of combinations of anxiety disorders in primary care outpatients.

Methods—1004 patients with panic disorder (PD), generalized anxiety disorder (GAD), social anxiety disorder (SAD) or posttraumatic stress disorder (PTSD) provided data on their mental and physical functioning, and disability. Multivariate regressions compared functional levels for patients with different numbers and combinations of disorders.

Results—42% of patients had one anxiety disorder only, 38% two, 16% three and 3% all four. There were few relative differences in functioning among patients with only one anxiety disorder, although those with SAD were most restricted in their work, social, and home activities and those with GAD were the least impaired. Functioning levels tended to deteriorate as comorbidity increased.

Conclusions—Of the four anxiety disorders examined, GAD appears to be the least disabling, although they all have more in common than in distinction when it comes to functional impairment. A focus on unique effects of specific anxiety disorders is inadequate, as it fails to address the more pervasive impairment associated with multiple anxiety disorders, which is the modal presentation in primary care.

Background

Anxiety disorders are among the most prevalent mental health disorders in the United States. About 18% of the US population will suffer from an anxiety disorder each year and almost 29% will experience an anxiety disorder at some point in their lives (Kessler et al., 2005). Prior studies of patients with specific anxiety disorders show they have large decrements in functioning and well-being and increases in disability compared to those without anxiety disorders (Blazer et al., 1991; Massion et al., 1993; Schneier et al., 1994; Katon et al., 1995; Sherbourne et al., 1996; Hollifield et al., 1997; Schoenfeld et al., 1997; Zatzick et al., 1997; Malik et al., 1999). These disabilities manifest themselves in the absence of desire to perform activities, interference in level of performance, and avoidance of activities. While the negative impact of anxiety is fairly well-established relative to that in persons without anxiety, few studies have compared differences in functioning and disability between the anxiety disorders themselves. In addition, while individuals with more than one anxiety diagnosis appear to have increased symptom severity (Kessler, Chiu et al., 2005), less is known about whether or not comorbidity affects levels of functioning and disability (Norberg et al., 2008), although some studies have found lower levels of quality of life (QOL) in anxiety patients with comorbid depression compared to those with anxiety alone (Stein & Kean 2000; Lochner et al., 2003). A recent meta-analysis found that, compared to control samples, no particular anxiety disorder diagnosis was associated with significantly poorer overall quality of life than was any other anxiety disorder diagnosis (Olatunji et al., 2007). However, there was difficulty in comparing across studies due to the use of different clinical settings, small sample sizes for many of the specific anxiety disorders, and different measures of QOL assessed.

This paper uses a large sample of primary care patients diagnosed with one or more of four common anxiety disorders (generalized anxiety disorder, panic disorder, social anxiety disorder, and posttraumatic stress disorder) to address these issues. Specifically, we estimate whether the relative impact of anxiety on functioning and disability is due to the principal anxiety disorder or to the co-occurrence with other anxiety disorders. In addition, we estimate the relative contribution to reduced functioning and increased disability of different combinations of anxiety disorders, controlling for the presence of co-morbid depression. We control for co-morbid depression since it is one of the most burdensome disorders worldwide (Murray and Lopez, 1996). Less is known about the comparative impact of the anxiety disorders themselves.

Method

Sample

Subjects include 1004 primary care patients with panic disorder (PD), social anxiety disorder (SAD), generalized anxiety disorder (GAD) or posttraumatic stress disorder (PTSD) enrolled between June 2006 and April 2008 in the Coordinated Anxiety Learning and Management (CALM) study. CALM is the largest randomized trial of collaborative care for anxiety disorders conducted to date (See Sullivan et al. 2007, for details about the study). It is a flexible delivery model for primary care anxiety treatment that simultaneously targets any of these four common anxiety disorders in primary care; provides strategies to enhance patient engagement in treatment, including allowing choice of either CBT, medication, or both; and provides the option for additional treatment over the course of a year in three month "steps". It utilizes a web based outcomes system to optimize treatment decisions and a computer-assisted program to allow CBT-inexperienced care managers to optimize delivery of CBT. Medication is prescribed by primary care physicians with care manager assistance in promoting adherence, dose optimization, and medication switches/augmentation.

Patient recruitment was coordinated at four sites: University of Washington, Seattle, University of California at San Diego and Los Angeles, and the University of Arkansas at Little Rock, Arkansas. Each of the four sites selected clinics in their geographic area to participate. Candidate clinics were evaluated and 17 were purposively selected based on a number of considerations, including provider interest, space availability, size and diversity of the patient population, and insurance mix (public and private).

A "facilitated referral" approach used multiple strategies to recruit subjects. Primary care providers and clinic nursing staff directly referred potential subjects, and sites actively publicized the study within each clinic, allowing for self-referral. In addition, at some sites, a simple five-question anxiety screener (Means-Christensen et al., 2006) was used to identify patients who had potential anxiety disorders.

Referred subjects met with a study clinical anxiety specialist to determine eligibility for CALM. An eligible subject had to be a patient at one of the participating clinics, be at least 18 years old, meet DSM-IV criteria for GAD, PD, SAD, or PTSD (based on the Mini International Neuropsychiatric Interview (Lecrubier et al., 1997) administered by a nurse or social worker after formal training and diagnostic reliability testing), score at least 8 (moderate but clinically significant anxiety symptoms on a scale ranging from 0–20) on the Overall Anxiety Severity And Impairment Scale (OASIS) (Campbell-Sills et al., 2009), be willing to participate in CALM, and be able to provide written, informed consent. The MINI has been shown to have high inter-rater and test-retest reliability and good concordance with the SCID and CIDI (Lecrubier et al., 1997; Sheehan et al., 1998). Exclusion criteria were minimal and were intended to exclude persons who would not likely benefit from the intervention or for whom the intervention could be risky. They included serious alcohol or drug use (specifically, alcohol or marijuana dependence or any other drug abuse or dependence, including methadone – 4% were excluded for this reason), unstable medical conditions, marked cognitive impairment, active suicidal intent or plan, psychosis, or bipolar I disorder. Subjects already receiving ongoing CBT were excluded. Finally, persons without routine access to a telephone, or who could not speak English or Spanish were excluded.

Of 1620 patients referred and interviewed for eligibility, 1062 were eligible and 1036 consented for the study. Data for the analyses in this paper are from the 1004 subjects who completed a baseline telephone questionnaire conducted by a centralized data collection facility at the RAND Corporation in Santa Monica, CA.

Measures

To measure functioning and disability status, we used five widely-used self-report measures. Mental and physical health-related quality of life were measured using the global physical (PCS12) and mental (MCS12) health scales of the short-form 12 (SF-12v2) (Ware et al., 2002). The SF-12 summary scores have internal consistency reliability estimates of 0.89 and 0.86, exceeding the minimum standard for group level comparisons and have demonstrated good validity for discriminating between groups differing in physical or mental health status (Ware et al., 2002). Norm-based scoring is used to achieve a mean of 50 and SD of 10 in the general US population for each measure. The three-item Sheehan Disability Index (SDI) was used to measure the extent to which work/school, social life and home life or family responsibilities were impaired by the patient's symptoms (Sheehan 1983). The internal consistency of the measure has been shown to be high (0.83) in primary care patients and it has been shown to be a sensitive tool for identifying primary care patients with mental-health related functional impairment (Leon et al., 1997). A more direct activity limitation measure was the CDC Healthy days measure (HD3-Day), a single-item estimate of restricted activity days or days (in the past 30) in which poor physical or mental health kept the subject from doing usual activities (CDC 2000). A number of studies have demonstrated the construct and known groups validity of this measure in various populations (Moriarty et al., 2003). Finally, the EQ-5D, the 5-item EuroQol preference based measure that evaluates health-related quality of life in the areas of mobility, self-care, usual activities, pain/discomfort, anxiety/depression (Rabin et al., 2001) was used to describe the patient's health status and preference for that health state on a scale of 0 to 1. A high score on this measure indicates greater preference for one's own current health state across the domains of physical, mental and social functioning. A wide range of studies have reported on the reliability and validity of the EQ-5D in countries around the world (Brooks et al., 2003). While the five measures are moderately correlated in our sample (e.g., the highest correlation is −.64 between MCS12 and the SDI), each provides unique information. MCS12 and PCS12 indicate more subjective reports of functioning or well-being, while the SDI and HD3-Day measures (correlation = .54) indicate disability more directly.

To test whether the effect of having one or more anxiety disorders was due to increased avoidance behavior or frequency/severity of anxiety, we included three OASIS items in our analyses: How often did you avoid situations, places, objects, or activities because of anxiety or fear? (avoidance item); How often have you felt anxiety? (frequency item); How intense or severe was your anxiety? (severity item) (Campbell-Sills et al., 2009). All multivariate analyses controlled for demographics (age, gender, education, ethnicity), number of self-report chronic medical conditions (asthma, high blood sugar or diabetes, hypertension or high blood pressure, arthritis or rheumatism, cancer, neurological condition, stroke or major paralysis, heart attack, back problems, stomach ulcer, chronic inflamed bowel, thyroid disease, kidney failure, migraine headaches, trouble seeing even with glasses, chronic lung disease, a physical disability), co-morbid depression, and study site.

Statistical Approach

Linear multivariate regression models were run to evaluate whether levels of functioning and disability were significantly different in subjects with one or more anxiety disorders (e.g., subjects with 1, 2 or 3+ disorders), controlling for demographics, number of chronic medical conditions, co-morbid depression, and study site. To examine whether avoidance or increased frequency and severity of anxiety explained these results, we conducted additional analyses adding the avoidance item singly to the multivariate regression models and then repeated the analyses with all three OASIS items in the model simultaneously. Similarly, linear multivariate regression models were run to evaluate the unique effect of PD, SAD and PTSD, entered simultaneously, compared to GAD also controlling for the other covariates. GAD was selected

as the comparator because it was the most frequent anxiety disorder. Evidence of an independent burden of disability for each anxiety disorder, after adjusting for other disorders simultaneously, provides additional support for increased burden due to comorbidity. To determine the relative contribution to reduced functioning and well-being of different combinations of anxiety disorders, regression models were subset to patients with one anxiety disorder only; two disorders; and three disorders. Indicators for type of disorder or combinations of disorders were included as independent variables in the relevant subset models, again controlling for covariates described above. Results are standardized predictions generated from parameter estimates in each regression model.

Results

The baseline sample of 1004 subjects was 71% female, 20% Hispanic, 12% black, 57% white, and 12% other ethnicity. Twenty two percent had not completed high school. The mean age was 43 years. Forty-two percent of the sample had one anxiety disorder only; 38% had two; 16% had three; and 3% had all four anxiety disorders. On average, the baseline sample reported 2.3 (out of 17) comorbid chronic medical conditions. Sixty-three percent were currently taking a prescribed psychotropic medication.

Table 1 describes the sample in terms of associated comorbid depression. As number of anxiety disorders increased, so did the percent with co-morbid depression. For example, 56% of those patients with only one anxiety disorder had co-morbid depression compared to 88% of those patients with 4 anxiety disorders. Co-morbid depression varied from 64% in subjects with PD to 85% in subjects with PTSD (with or without another anxiety disorder).

Table 2 shows baseline levels of functioning and well-being for all CALM subjects combined. For comparison purposes, the last column indicates general population means based on published literature. On all but physical health, CALM subjects showed reduced levels of functioning and well-being and/or increased levels of disability from those normally found in general populations.

Table 3 shows baseline levels of functioning and well-being by number of co-morbid anxiety disorders. Functioning and preferences for health states decrease while activity limitations and disability increase as number of anxiety co-morbidities increase. Almost all comparisons are significantly different from one another except that patients with 2–4 anxiety disorders have similarly low levels of mental well-being, and patients with 1 or 2 anxiety disorders have similarly high levels of physical functioning.

The number of comorbid anxiety disorders correlated 0.13 with the OASIS frequency item, 0.19 with the OASIS severity item, and 0.24 with the OASIS avoidance item. When the OASIS avoidance item was included in the models, nine out of the 12 significant comparisons shown in Table 3 remained significant. The differences between patients with 2 anxiety disorders and those with 3–4 disorders were reduced for the two disability measures (Sheehan and HD3-Day), while the difference between patients with 1 disorder only and those with 2 disorders was also reduced for the HD3-Day disability measure. When the OASIS frequency and severity items were included along with avoidance two more comparisons became non-significant: The difference between patients with 1 and 2 disorders on the EQ5-D and the difference between patients with 1 and 3–4 disorders on the MCS12.

Table 4 shows parameter estimates from regression models where PD, SAD, and PTSD were entered simultaneously with GAD, the most prevalent disorder, as the comparator. Patients with SAD had significantly lower mental functioning relative to GAD, controlling for the other anxiety disorders, depression, chronic medical conditions and demographics. Patients with either PD or PTSD had significantly lower physical functioning relative to GAD. Disability

was significantly less in GAD compared to each of the other anxiety disorders, while preference for current health state was significantly higher/better in GAD compared to each of the other anxiety disorders.

Table 5 shows baseline levels of functioning and well-being among patients with only one anxiety disorder, with two disorders or with three disorders. There were few large differences among these patients. Among patients with only one disorder, those with PD reported the highest level of mental well-being but lowest level of physical functioning. Patients with SAD had the highest disability levels and, along with patients with PTSD, the most days of activity limitation due to health.

Among patients with two anxiety disorders, those with PD comorbid with SAD appeared worse off on 3 out of 5 measures, although not all comparisons were statistically significantly different from one another. GAD combined with one other comorbid anxiety diagnosis appeared to be the least limiting combination.

Finally, among patients with 3 anxiety disorders, in almost all comparisons, the groups appeared equally low in levels of functioning and well-being. The combinations with GAD appeared least limiting, although not significantly so except for the Sheehan Disability Index.

Discussion

All measures of functioning and disability, except for physical functioning, showed substantial impairment in the overall sample compared to general population norms. This finding is consistent with that of many other studies that have shown increased disability and poor mental health outcomes in persons with anxiety, relative to non-anxious controls (Markowitz et al., 1989; Noyes 1990; Klerman et al., 1991; Fifer et al., 1994). It is also consistent with our prior work on a different primary care sample which showed less impact of anxiety disorders on physical health functioning than on mental health functioning (Stein et al., 2005)

In this primary care sample of patients with anxiety disorders, co-morbidity was high with 58 percent of the sample diagnosed with more than one anxiety disorder. Co-morbid depression was also high. It was highest in patients with posttraumatic stress disorder (PTSD) and increased substantially to almost 88 percent as the number of comorbid anxiety disorders increased. Such high comorbidity is common in primary care patients (Kroenke et al., 2007) and, based on primary care provider feedback about the desirability of coordinating care for all anxiety disorders, was one of the reasons the CALM intervention was designed to address multiple disorders simultaneously.

The burden of disability is clearly greater as the number of anxiety comorbidities increases. This was reflected in the linear relationship (especially in increased levels of disability and the decreasing health-related quality of life as measured by the EQ-5D) as one moves from having one disorder alone to having multiple disorders. Several other studies have confirmed the dose-response relationship between number of comorbidities and disability (Andrews et al., 2002; Kroenke et al., 2007). The question remains as to why increased comorbidity leads to increased disability and poorer functioning. It may be that the number of comorbidities is merely a marker for severity. Alternatively, as number of comorbid anxiety disorders increase, avoidance behavior is likely to increase. In this study, the number of comorbid anxiety disorders correlated significantly with the OASIS avoidance item. When the avoidance item was added to the multivariate analyses three out of 12 comparisons were mediated (i.e., differences were reduced) by the addition of the item, suggesting that avoidance partially explains the relationship between number of comorbid disorders and poor outcomes. Perhaps not surprisingly, the outcomes affected were disability outcomes including days kept from doing usual activities (as measured by the CDC Healthy Days measure) and disruption in specific

areas of work, social life and family responsibilities (as measured by the Sheehan Disability Index). When frequency and severity of anxiety were added to the multivariate analyses, two more generic health-related quality of life outcomes were affected: mental health functioning and the integrative preference-based EQ-5D measure. Despite these reductions in differences, the burden of disability remained greater as the number of anxiety disorders increased for the majority of analyses. Thus, neither frequency, nor severity of anxiety, nor extent of avoidance completely explains the observed relationships. Other factors, such as third variable correlates of comorbidity (e.g., SES, interpersonal dysfunction) may play a role and need to be examined in future research.

Even when controlling for all anxiety disorders simultaneously, we found significant unique effects of each anxiety disorder relative to GAD alone, again confirming that disability increases with added disorders. While GAD itself is also impairing, these results suggest that it is the least impairing of the four disorders measured in this study. There may be several reasons for this finding. It may be due to a lower diagnostic threshold for GAD because it does not include behavioral interference or avoidance. However, recent results from an Australian general population sample found that diagnostic thresholds for social phobia and obsessive compulsive disorder were less stringent than for GAD (Andrews et al., in press). This raises the possibility that there might be a bias in the kinds of patients primary care providers refer for anxiety treatment. Providers may be more attuned to GAD (which was the most prevalent anxiety disorder in this study) and hence refer people with GAD who are, on average, less ill than are those primary care patients with the other anxiety disorders. In order to be identified and therefore referred to the CALM study, patients with PD, SAD or PTSD may have been more ill than patients with GAD.

We found interesting trends when subsetting the sample according to number of anxiety disorders. In general, in contrast to studies of depression-related functioning (Wells et al., 1996), physical functioning did not appear to be affected greatly by the presence of anxiety, although levels were reduced in patients with PD alone and in some combinations of comorbidities which included PD. The effect sizes as seen in Table 5 were not large, however, with physical functioning levels in those with panic disorder (with and without other comorbidities) from one-fourth to one-half a standard deviation below the general population norm of 50. It may be that the often comorbid agoraphobia associated with PD affects mobility and therefore contributes to the decreased physical functioning in patients with PD. In addition, decreased physical functioning in PD patients may be a consequence of avoidance of physical sensations.

Patients with SAD alone were severely restricted in work/social/home activities and spent more days limited in activities, as did those with PTSD. The combination of social anxiety and PD appeared particularly debilitating and patients with both conditions had the lowest rating of their overall health-related quality of life, as measured by the EQ-5D. These findings for SAD reinforce the seriousness of this condition in which fear of negative evaluation by others causes such individuals to avoid situations in which scrutiny will take place, whether in the work force, socially or at home (Stein & Stein 2008). Given that SAD is the third most prevalent psychiatric disorder (after depression and alcohol abuse) in the community (Kessler et al., 1994; Magee et al., 1996) and is associated with extreme disability (Kessler 2003) and substantial unmet need for care (Roy-Byrne and Stein 2005), awareness of the seriousness of this disorder should be promoted. Further screening and outreach programs may be needed to identify these patients and facilitate their access to treatment (Roy-Byrne and Stein 2005).

Our results are limited by the fact that the sample was for the most part referred to the study by primary care physicians and thus, because they had been detected by their physician, may represent a more seriously ill population than that found if screened in the primary care

population. However, the inferences on relative impact and dose-response relationship between number of comorbidities and disability should be valid. Our results are also limited by the relatively small sample with posttraumatic stress disorder which may have made it difficult to detect significant differences between this group and patients with other anxiety disorders. However, patients with PTSD were significantly worse off on four of our five functioning and disability measures than patients with GAD and they did have the highest levels of activity limitation both when considered alone and in combination with other disorders underscoring the seriousness of this disorder also. Finally, because of the number of tests conducted, some of the observed significant results in Table 5 might be due to chance. It is possible that other indices of psychopathology such as the presence of Axis II disorder(s) might also explain some of the disability attributable to anxiety disorders. This is an area worthy of additional research.

Results from this study are relevant to the primary care clinicians who treat such patients. Clinicians should be aware of the substantial comorbidity among the anxiety disorders and with depression and the fact that there is a greater burden on those with multiple disorders. The literature is, at present, unclear as to whether or not the presence of multiple disorders requires a different therapeutic approach that broadly tackles the comorbid conditions. There is, however, some literature suggesting that treating one disorder with CBT can have a very positive effect on surrounding comorbidities (e.g., Tsao, Mystkowski, Zucker & Craske, 2002; Craske, Farchione, Allen, Barrios, Stoyanova, Rose, 2007). Results from our CALM study may help resolve this controversy.

In conclusion, patients with anxiety disorders seen by primary care clinicians have serious disability and low functioning even after adjusting for co-morbid depression (and number of chronic medical conditions). Clinicians should be vigilant for multiple anxiety disorders and comorbid depression in patients suspected to have any of these four anxiety disorders. In addition, clinicians should be more attuned to patients with social anxiety disorder and recognize the seriousness of this condition. Effective treatments are available for all of these anxiety disorders and effective methods of identifying and treating them need to be incorporated into standard care practices.

Acknowledgments

References

Andrews G, Slade T, Issakidis C. Deconstructing current comorbility: data from the Australian National Survey of Mental health and Well-Being. British Journal of Psychiatry 2002;181:306–314. [PubMed: 12356657]

Andrews G, Sunderland M, Kemp A. The consistency of diagnostic thresholds in DSM-V. Australian and New Zealand Journal of Psychiatry. 2009 in press.

Blazer, DG.; Hughes, D.; George, LK.; Swartz, M.; Boyer, R. Generalized anxiety disorder. In: Robins, LN.; Regier, DA., editors. Psychiatric Disorders in America: The Epidemiologic Catchment Area Study. New York: Free Press; 1991. p. 180-203.

Brooks, R.; Rabin, R.; de Charro, F., editors. The Measurement and Valuation of Health Status Using EQ-5D: A European Perspective. Kluwer Academic Publishers; The Netherlands: 2003.

Campbell-Sills L, Norman SB, Craske MB, Sullivan G, Lang AJ, Chavira DA, Sherbourne C, Roy-Byrne P, Stein MB. Validation of a Brief Measure of Anxiety-Related Severity and Impairment: The Overall Anxiety Severity and Impairment Scale (OASIS). Journal of Affective Disorders 2009;11:92–101. [PubMed: 18486238]

Centers for Disease Control and Prevention. Measuring Healthy Days. Atlanta, Georgia: CDC; 2000.

Craske MG, Farchione TJ, Allen LB, Barrios V, Stoyanova M, Rose R. Cognitive behavioral therapy for panic disorder and comorbidity: More of the same or less of more? Behaviour Research and Therapy 2007;45:1095–1109. [PubMed: 17069753]

Fifer SK, Mathias SD, Patrick DL, Mazonson PD, Lubeck DP, Buesching DP. Untreated anxiety among adult primary care patients in a health maintenance organization. Archives of General Psychiatry 1994;51:740–750. [PubMed: 8080351]

Hansson L. Quality of life in depression and anxiety. International Review of Psychiatry 2002;14:185–189.

Hollified M, Katon W, Skipper B, Chapman T, Ballenger JC, Mannuzza S, Fyer AJ. Panic disorder and quality of life: variables predictive of functional impairment. American Journal of Psychiatry 1997;154:766–772. [PubMed: 9167503]

Katon W, Hollifield M, Chapman T, Mannuzza S, Ballenger J, Fyer A. Infrequent panic attacks: psychiatric comorbidity, personality characteristics and functional disability. Journal of Psychiatric Research 1995;29:121–131. [PubMed: 7666380]

Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M, Eshleman S, Wittchen H-U, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the National Comorbidity Survey. Archives of General Psychiatry 1994;51:8–19. [PubMed: 8279933]

Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Archives of General Psychiatry 2005;62(6):593–602. [PubMed: 15939837]

Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey replication. Archives of General Psychiatry 2005;62:617–709. [PubMed: 15939839]

Kessler RC. The impairments caused by social phobia in the general population: Implications for intervention. Acta Psychiatica Scandinavica 2003;108(Suppl 417):19–17.

Klerman GL, Weissman MM, Ouellette R, Johnson J, Greenwald S. Panic attacks in the community: social morbidity and health care utilization. Journal of the American Medical Association 1991;265:742–746. [PubMed: 1990190]

Kroenke K, Spitzer RL, Williams JBW, Monahan PO, Lowe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Annals of Internal Medicine 2007;146:317–325. [PubMed: 17339617]

Lecrubier Y, Sheehan DV, Weiller E, Amorim P, Bonora I, Sheehan KH, Janavs J, Dunbar GC. The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: Reliability and validity according to the CIDI. European Psychiatry 1997;12(5):224–231.

Leon AC, Olfson M, Portera L, Farber L, Sheehan DV. Assessing impairment in primary care: a psychometric analysis of the Sheehan Disability Scale. Int J Psychiatry Med 1997;27:93–105. [PubMed: 9565717]

Lochner C, Mogotsi M, du Toit PL, Kaminer D, Niehaus DJ, Stein DJ. Quality of life in anxiety disorders: A comparison of obsessive–compulsive disorder, social anxiety disorder, and panic disorder. Psychopathology 2003;36:255–262. [PubMed: 14571055]

Luo N, Johnson G, Shaw J, Feeney D, Coons SJ. Self-reported health status of the general adult US population as assessed by the EQ-5D and Health Utilities Index. Medical Care 2005;43(11):1078–1086. [PubMed: 16224300]

Magee WJ, Eaton WW, Wittchen HU, McGonagle KA, Kessler RC. Agoraphobia, simple phobia and social phobia in the National Comorbidity survey. Archives of General Psychiatry 1996;53:159–168. [PubMed: 8629891]

Malik ML, Connor KM, Sutherland SM, Smith RD, Davison RM, Davidson JR. Quality of life and posttraumatic stress disorder: a pilot study assessing changes in SF-36 scores before and after treatment in a placebo-controlled trial of fluoxetine. Journal of Traumatic Stress 1999;12:387–393. [PubMed: 10378176]

Markowitz J, Weissman M, Ouellette R, Lish J, Klerman GL. Quality of life in panic disorder. Archives of General Psychiatry 1980;46:984–992. [PubMed: 2684086]

Massion AO, Warshaw MG, Keller MB. Quality of life and psychiatric morbidity in panic disorder and generalized anxiety disorder. American Journal of Psychiatry 1993;150:600–607. [PubMed: 8465877]

Means-Christensen AJ, Sherbourne CD, Roy-Byrne PP, Craske MG, Stein MB. Using five questions to screen for five common mental disorders in primary care: The anxiety and depression detector (ADD). General Hospital Psychiatry 2006;28(2):108–118. [PubMed: 16516060]

Moriarty DG, Zack MM, Kobau R. The Cennters for Disease control and Prevention's Healthy Days Measures – Population tracking of perceived physical and mental health over time. Health and Quality of Life Outcomes 2003;I:37. [PubMed: 14498988]

Murray, CJ.; Lopez, AD. Injuries and Risk Factors in 1990 and Projected to 2020. Harvard University Press; Cambridge, MA: 1996. The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases.

Norbeg MM, Diefenbach GJ, Tolin DF. Quality of life and anxiety and depressive disorder comorbidity. Journal of Anxiety Disorders 2008;22:1516–1522. [PubMed: 18424062]

Noyes R. The comorbidity and mortality of panic disorder (1990). Psychiatric Medicine 8:41–66. [PubMed: 2185502]

Olatunji BO, Cisler JM, Tolin DF. Quality of life in the anxiety disorders: a meta-analytic review. Clinical Psychology Review 2007;27:572–581. [PubMed: 17343963]

Olfson M, Fireman B, Weissman MM, Leon AC, Sheehan DV, Kathol RG, Hoven C, Farber L. Mental disorders and disability among patients in a primary care group practice. Am J Psychiatry 1997;154:1734–1740. [PubMed: 9396954]

Rabin R, deCharro F. EQ-5D: A measure of health status from the EuroQol Group. Annals of Medicine 2001;33:337–343. [PubMed: 11491192]

Roy-Byrne P, Stein M. Social anxiety in primary care: hidden in plain view? General Hospital Psychiatry 2005;27:155–157. [PubMed: 15882760]

Schonfeld WH, Verboncoeur CJ, Fifer SK, Lipschutz RC, Lubeck DP, Buesching DP. The functioning and well-being of patients with unrecognized anxiety disorders and major depressive disorder. Journal of Affective Disorders 1997;43:105–119. [PubMed: 9165380]

Schneier FR, Heckelman LR, Garfinkel R, Campeas R, Fallon BA, Gitow A, Street L, DelBene D, Liebowitz MR. Functional impairment in social phobia. Journal of Clinical Psychiatry 1994;55:322–331. [PubMed: 8071299]

Sheehan, D. The Anxiety Disease. New York: Scribner; 1983.

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E. The Mini International Neuropsychiatric Interview (MINI): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry 1998;59 (Suppl 20): 22–33. [PubMed: 9881538]

Sherbourne CD, Wells KB, Judd LL. Functioning and well-being of patients with panic disorder. American Journal of Psychiatry 1996;153:213–218. [PubMed: 8561201]

Stein MB, Roy-Byrne PP, Craske MG, Bystritsky A, Sullivan G, Pyne JM, Katon W, Sherbourne CD. Functional impact and health utility of anxiety disorders in primary care outpatients. Medical Care 2005;43:1164–1170. [PubMed: 16299426]

Stein MB, Kean YM. Disability and quality of life in social phobia: Epidemiologic findings. American Journal of Psychiatry 2000;157:1606–1613. [PubMed: 11007714]

Stein MB, Stein DJ. Social anxiety disorder. Lancet 2008;371:1115–1125. [PubMed: 18374843]

Sullivan G, Craske MG, Sherbourne C, Edlund M, Rose R, Golinelli D, Chavira DA, Bystritsky A, Stein MB, Roy-Byrne PP. Design of the Coordinated Anxiety Learning and Management (CALM) study: innovations in collaborative care for anxiety disorders. General Hospital Psychiatry 2007;9:379–387. [PubMed: 17888803]

Tsao JCI, Mystkowski JL, Zucher BG, Craske MG. Impact of cognitive-behavioral therapy for panic disorder on comorbidity: a controlled investigation. Behaviour Research and Therapy 2005;43:959–970. [PubMed: 15896289]

Ware, JE., Jr; Kosinski, M.; Turner-Bowker, D.; Gandek, B. How to score version 2 of the SF-12 Health Survey (with a Supplement Documenting Version 1). Lincoln, RI: QualityMetric Incorporated; 2002.

Weiller E, Bisserbe JC, Boyer P, Lepine JP, Lecrubier Y. Social phobia in general health care: an unrecognized undertreated disabling disorder. British Journal of Psychiatry 1996;168:169–174. [PubMed: 8837906]

Wells, KB.; Sturm, R.; Sherbourne, CD.; Meredith, LS. Caring for Depression. Harvard University Press; Cambridge, Massachusetts: 1996.

Zatzick DF, Marmar CR, Weiss DS, Browner WS, Metzler TJ, Golding JM, Stewart A, Schlenger WE, Wells KB. Posttraumatic stress disorder and functioning and quality of life outcomes in a nationally representative sample of male Vietnam veterans. American Journal of Psychiatry 1997;154:1690–1695. [PubMed: 9396947]

Table 1

Co-Morbid Depression by Number and Type of Anxiety Disorder

# Anxiety Disorders	N(%)	% MDD
1	421 (42)	56%
2	387 (38)	64%
3	162 (16)	81%
4	34 (03)	88%
Type of Anxiety Disorder		
PD	475 (47)	64%
GAD	756 (75)	68%
SAD	405 (40)	69%
PTSD	181 (18)	85%

MDD = Major Depressive Disorder; PD = Panic Disorder; GAD = Generalized Anxiety Disorder; SAD = Social Anxiety Disorder; PTSD = Posttraumatic Stress Disorder

Table 2

Baseline levels of Functioning and Well-Being for CALM Subjects (N=1004)

Measure	Range	CALM Subjects Mean (SD)	General Population Mean
Mental Health SF-12 Composite (+)	0–100	31.8 (10.0)	50[a]
Physical Health SF-12 Composite (+)	0–100	49.2 (11.5)	50[a]
Sheehan Disability Index (−)	0–30	17.0 (7.3)	(5–6)[b]
Days of Activity Limitation (−)	0–30	11.3 (9.8)	2.2[c]
EuroQol EQ-5D (+)	0–1	0.67 (0.20)	0.87[d]

Note a − or + indicates direction of good health

[a] The Mental and Physical Health composite scores reflect norm-based scoring where the mean of the general population is 50 with a standard deviation of 10.

[b] Primary care population norms (Leon et al., 1997; Olfson et al., 1997).

[c] 2008 nationwide mean days of activity limitation (CI 2.1–2.3) are available on the CDC website http;//www.cdc.gov.hrqol/.

[d] US general population mean (Luo et al., 2005)

Table 3

Functioning and Well-Being Levels by Number of Anxiety Disorders

	Number of Anxiety Disorders		
Measure	**1**	**2**	**3–4**
	Mean (SE)	**Mean (SE)**	**Mean (SE)**
Mental Health SF- 12 Composite (+)	33.1(0.4)[a]	31.3(0.4	30.1(0.6)
Physical Health SF- 12 Composite (+)	50.3(0.5)[b]	49.0(0.5)	47.3(0.7)
Sheehan Disability Index (−)	15.5(0.3)	17.5(0.3)[c]	19(0.5)[c,d]
Days of Activity Limitation (−)	10.1(0.4)	11.4(0.5)[e]	13.6(0.7)[f]
EuroQol EQ-5D (+)	0.699(.009)[g]	0.664(.009)[h]	0.605(.014)

Note: Analyses controlled for age, gender, education, ethnicity, number of self-report chronic medical conditions, comorbid depression and study site.

[a]Significantly higher than subjects with 2 (p=.004) or 3–4 (p=.002) anxiety disorders

[b]Significantly higher than subjects with 3–4 (p=.001) anxiety disorders

[c]Significantly higher than subjects with 1 (p=.00001) anxiety disorder

[d]Significantly higher than subjects with 2 (p=.0103) anxiety disorders

[e]Significantly higher than subjects with 1 (p=.0428) anxiety disorder

[f]Significantly higher than subjects with 1 (p<.0000) or 2 (p=.0084) anxiety disorders

[g]Significantly higher than subjects with 2 (p=.007) or 3–4 (p=.0000) anxiety disorders

[h]Significantly higher than subjects with 3–4 (p=.003) anxiety disorders

Table 4

Unique Effect of Each Anxiety Disorder Relative to GAD

Dependent Variable	PD	SAD	PTSD
	β (T-value, p)	β (T-value, p)	β (T-value, p)
Mental Health SF- 12 Composite (+)	−1.03 (−1.80, .07)	−2.16 (−3.79, .0002)	−0.14 (−.19, .85)
Physical Health SF- 12 Composite (+)	−2.45 (−3.87, .0001)	0.08 (0.14, .89)	−3.90 (−4.75, .0001)
Sheehan Disability Index (−)	1.18 (2.76, .006)	2.72 (6.37, .0001)	1.22 (2.18, .029)
Days of Activity Limitation (−)	1.58 (2.68, .008)	1.82 (3.09, .002)	4.34 (5.63, .0001)
EuroQol EQ-5D (+)	−.06 (−4.83, .0001)	−.03 (−2.40, .017)	−.05 (−3.46, .0006)

Note: Analyses controlled for age, gender, education, ethnicity, number of self-report chronic medical conditions, comorbid depression and study site.

Table 5

Functioning and Well-Being Levels in Patients with One, Two or Three Anxiety Disorders

	Mental Health SF-12Composite (+) Mean (SE)	Physical Health SF-12Composite (+) Mean (SE)	Sheehan Disability Index (−) Mean (SE)	Days of Activity Limitation (−) Mean (SE)	EuroQol EQ-5D (+) Mean (SE)
One Anxiety Disorder					
PD (N=100)	35.7(0.9)[a]	48.6(1.0)[c]	14.0(0.7)[d]	9.9(.9)[f]	0.709(.018)
GAD (N=256)	34.0(0.6)[b]	51.0(0.6)	14.8(0.4)[e]	8.6(.5)[g,h]	0.713(.011)
SAD (N=51)	31.2(1.2)	51.4(1.4)	17.4(1.0)	12.7(1.2)	0.692(.024)
PTSD (N=14)	34.4(2.4)	50.2(2.6)	14.8(1.9)	14.9(2.3)	0.658(.045)
Two Anxiety Disorders					
PD+GAD (N=143)	30.8(0.7)	49.1(0.8)	16.8(0.5)	10.4(.8)[m]	0.644(.016)
PD+SAD (N=40)	29.8(1.4)	46.7(1.5)	20.5(1.0)[l]	14.5(1.5)	0.605(.031)
PD+PTSD (N=17)	30.4(2.1)	44.6(2.4)	18.1(1.6)	16.3(2.3)	0.618(.047)
GAD+SAD (N=137)	31.2(0.7)	51.3(0.8)[j]	17.8(0.5)	10.1(.8)[m]	0.705(.016)[n]
GAD+PTSD (N=38)	34.8(1.4)[i]	46.8 (1.6)[k]	16.1(1.0)	12.4(1.5)	0.694(.031)[o]
SAD+PTSD (N=12)	33.4(2.4)	47.5(2.8)	16.4(1.8)	16.4(2.7)	0.668(.056)
Three Anxiety Disorders					
PD+GAD+SAD (N=96)	28.1(1.0)	48.9(1.1)[p]	19.7	13.4(1.0)	0.598(.01)
PD+GAD+PTSD (N=31)	29.7(1.7)	44.2(2.0)	18.4	15.9(1.8)	0.581(.035)
PD+SAD+PTSD (N=14)	25.8(2.8)	43.3(3.2)	24[q]	18.3(2.9)	0.588(.057)
GAD+SAD+PTSD (N=21)	27.1(2.1)	45.5(2.4)	21.5	15.7(2.2)	0.558(.042)

Note: Analyses controlled for age, gender, education, ethnicity, number of self-report chronic medical conditions, comorbid depression and study site.

[a] Significantly different p=.0035 from SAD

[b] Significantly different p=.0481 from SAD

[c] Significantly different p=.0483 from GAD

[d] Significantly different p=.006 from SAD

[e] Significantly different p=.0203 from SAD

[f] Significantly different p=.0419 from PTSD

[g] Significantly different p=.0068 from PTSD

[h] Significantly different p=.0027 from SAD

[i] Significantly higher than all other combinations except for SAD+PTSD and PD+PTSD

[j] Significantly higher than PD+SAD and PD+PTSD

[k] Significantly lower than GAD+SAD

[l] Significantly higher than all combinations except for PD+PTSD

[m] Significantly lower than PD+SAD, PD+PTSD, and SAD+PTSD

[n] Significantly higher than PD+GAD and PD+SAD

[o] Significantly higher than PD+SAD

[p] Significantly higher than PD+GAD+PTSD (p=.0433)

[q] Significantly higher than PD+GAD+SAD (p=.0347) and PD+GAD+PTSD (p=.0143)