Research Review

HUMAN AND ECONOMIC BURDEN OF GENERALIZED ANXIETY DISORDER

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The goal of the current work is to provide a comprehensive review and interpretation of the literature on the human and economic burden of generalized anxiety disorder (GAD) and how it compares with that of other mental disorders. The term "human burden" is used to describe quantified impairments in role functioning and quality of life (QOL). "Economic burden" describes costs related to health care resource utilization and lost work. A review of 34 studies reporting original quantitative data on associations between GAD and role functioning, QOL, and/or economic costs was undertaken. GAD was defined by DMS-III-R, DSM-IV, or ICD-10 DCR. Persons with GAD (both with and without a comorbid mental disorder) described significant impairments due to both physical and emotional problems. Studies typically showed that role and QOL impairments of GAD were at least comparable in magnitude to those of other anxiety disorders, somatoform disorders, and physical conditions, and greater than those of substance use disorders. Large representative studies showed that role impairments of pure GAD were similar in magnitude to those of pure MDD. Studies of DSM-IV disorders showed that QOL impairments of GAD were at least comparable in magnitude to those of MDD; studies of DSM-III-R disorders showed the opposite pattern. GAD was associated with considerable economic costs owing to lost work productivity and high medical resource use. Quality of care initiatives that have been implemented to increase recognition and improve treatment outcomes for persons with MDD should be extended to the effective management of GAD. Depression Anxiety 25:72–90, 2008. *© 2006 Wiley-Liss, Inc.*

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This literature review examines aspects of the human and economic burden of generalized anxiety disorder (GAD). The first objective was to consolidate what is known about the independent associations between GAD and impairments in role functioning and quality of life (QOL). The terms "role functioning" and "QOL" together encompass concepts of social, family, and occupational functioning, perceived emotional and physical health status, well-being and satisfaction with aspects of daily life; impairments in these areas are referred to as "human burden" in the current review. The second objective was to describe the economic costs of GAD related to use of health care resources and lost work. The third objective was to compare how the human and economic burden of GAD compares with that of other mental disorders.

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GAD is characterized by persistent worry and a number of mental and somatic symptoms that occur more days than not for a period of at least 6 months

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[APA, 1980, 1994; WHO, 1993]. Persons with GAD feel worried, tense, or apprehensive most of the time about everyday events and activities [APA, 1980, 1994; WHO, 1993]. Common symptoms can include restlessness and inability to relax, fatigue, sleep disturbance, irritability, muscle tension, muscle aches, headache, chest pain, and other types of pain [APA, 1980, 1994; WHO, 1993]. Persons with GAD may describe or emphasize either the worry or the somatic effects of chronic tension [Ballenger et al., 2001]. Consequently, the clinical presentation of GAD can differ markedly, depending on whether patients emphasize mental or somatic anxiety symptoms [Ballenger et al., 2001].

GAD affects ~5.7% of the population at some point in life [Kessler et al., 2005a] and is the most common anxiety disorder in primary care [Ormel et al., 1994; Wittchen et al., 2002]. The majority of persons with GAD experience at least one other mental disorder at some point, most commonly major depressive disorder (MDD) [Massion et al., 1993; Stein, 2001; Wittchen et al., 1994]. Persons with GAD also frequently experience comorbid physical disorders (e.g., peptic ulcer disease, diabetes, and irritable bowel syndrome), as well as cardiac and other somatic symptoms that often have no identifiable physiologic etiology [Carter and Maddock, 1992; Goodwin and Stein, 2002; Grigsby et al., 2002; Kane et al., 1988; Louge et al., 1993; Lydiard, 2000; Lydiard et al., 1993; Pearce et al., 1990; Roy-Byrne and Wagner, 2004]. If left untreated, GAD tends to follow a chronic course with periodic exacerbations [Ballenger et al., 2001; Wittchen et al., 2003]. Typically, persons with GAD experience symptoms for 5–10 years before receiving a diagnosis and treatment [Ballenger et al., 2001].

The significance of GAD has been a source of debate [Breier et al., 1985; Kessler, 2000; Kessler et al., 1999, 2002; Massion et al., 1993; Olfson et al., 1997]. An issue central to this debate is whether or not GAD is uniquely associated with impaired role functioning and QOL. A primary research question has been whether impairments of GAD are due to the disorder itself as opposed to MDD and/or other disorders that commonly co-occur with it. A related research question has been whether persons with GAD are substantially more impaired than persons without the disorder. If so, empirical findings would support the importance of recognizing and treating GAD, whether or not it is part of a comorbid condition.

In consolidating information about the burden of GAD, it is important to describe how GAD-related impairments compare with those of other mental disorders. It is also important to describe economic costs associated with GAD sufferers' use of health care services and lost work. Information about how GAD contributes to the overall human and economic burden of mental disorders can assist decision makers in determining how to allocate scarce health care resources and how to prioritize treatment of GAD in their health care agendas. For example, recognition of MDD as a particularly burdensome disorder has led to the development of targeted educational campaigns and disease management programs. These initiatives appear to be associated with positive clinical outcomes [Greenfield et al., 2000; Ofman et al., 2004; Olfson et al., 2002; Wang et al., 2005].

This literature review consolidates quantitative evidence on the human and economic burden of GAD by addressing three questions: What is known about associations between GAD and aspects of role functioning and QOL? What is known about the economic costs of GAD? How does the burden of GAD compare with that of other disorders?

MATERIALS AND METHODS

A literature search was performed in the MEDLINE and PsychLIT electronic databases for the reference period 1990 to 2005. Search terms included: "generalized or generalised anxiety disorder" and "burden, disability, impairment, quality of life, work, utilization, primary care, specialties medical, economic and cost." Reference lists of published articles were also handsearched. Peer-reviewed studies published in English were included in the current review if they reported original, quantitative data on associations between GAD and role functioning, QOL, and/or economic costs due to use of health care resources or lost work productivity. Clinical trials of GAD were included if they assessed role functioning or QOL with a validated measure. Studies examining the cost-effectiveness of alternative treatments for GAD were not considered. Studies must have defined GAD using one of three diagnostic classification systems that require a 6-month symptom duration to diagnose the disorder: the DSM-III-R [APA, 1980], DSM-IV [APA, 1994], or ICD-10 Diagnostic Criteria for Research [WHO, 1993]. ICD-10 DCR is hereafter referred to as ICD-10 for parsimony. ICD-10 places a greater emphasis on somatic symptoms of GAD than the DSM systems.

This review summarizes data from 34 studies that satisfied the inclusion criteria described above (Table 1). Of these, 31 studies measured role functioning and/or QOL among persons with GAD in the general community ($n = 12$), primary care ($n = 10$), and mental health settings ($n = 9$) (Table 1). The majority ($n = 9$ of 15) of studies based QOL assessment on the MOS 36-item short-form health survey (SF-36) [Ware and Sherbourne, 1992] (Table 1). Table 2 describes the SF-36. Three studies ($n = 3$) examined the economic burden of GAD related to use of health care resources and lost work productivity/absenteeism (Table 1). Studies on GAD often examined at least one other disorder, particularly MDD. This review describes how findings on the burden of GAD compare with those of the other disorder(s).

A variety of methods were used to examine how GAD (and the other disorder[s]) were associated with

TABLE 1. Summary of diagnostic classification system and outcome(s) assessed in thirty-four studies examining role functioning, QOL, and/or economic costs of GAD

		Role functioning[a]							
Setting reference	Classification system	Impairment days[d]	Social	Family	Work	Overall	Physical	QOL[b]	Cost[c]
General population									
Judd et al., 1998	DSM-III-R		X						
Wittchen et al., 1994	DSM-III-R					X			
Kessler et al., 1999	DSM-III-R	X	X						
Kessler et al., 2002	DSM-III-R	X							
Stein et al., 2004	DSM-III-R							X	
Cramer et al., 2005	DSM-III-R							X	
Bijl and Vaveli, 2000	DSM-III-R							X[e]	
Wittchen et al., 2000	DSM-III-R	X				X		X[e]	
Sanderson and Andrews, 2002	DSM-IV							X[e]	
Hunt et al., 2004	DSM-IV	X				X		X[e]	
Andrews et al., 2000	ICD-10							X[e]	
Kessler et al., 2005	DSM-IV					X			
Greenberg et al., 1999	DSM-III-R								X
Andlin-Sobocki et al., 2005	DSM-IV								X
Primary care									
Olfson et al., 1997	DSM-IV	X		X		X			
Olfson et al., 2000	DSM-IV	X		X		X			
Wittchen et al., 2002	DSM-IV	X							
Ormel et al., 1994	ICD-10	X			X		X		
Weiller et al., 1998	ICD-10	X	X						
Maier et al., 2000	ICD-10		X						
Schonfeld et al., 1997	DSM-III-R							X[e]	
Spitzer et al., 1995	DSM-III-R/ DSM-IV							X[e]	
Jones et al., 2001	DSM-IV							X[e]	
Mental health									
Massion et al., 1993	DSM-III-R							X	
Kennedy et al., 2002	DSM-III-R		X	X	X				
Mavissakalian and Zamar, 2000	DSM-III-R		X	X	X				
Wetherell et al., 2004	DSM-IV							X[e]	
Diefenbach et al., 2003	DSM-IV							X	
Souetre et al., 1994	DSM-III-R								X
Clinical Trials									
Pollack et al., 2001	DSM-IV					X			
Rosenthal, 2003	DSM-IV					X			
Rickels et al., 2003	DSM-IV					X			
Allgulander et al., 2004	DSM-IV				X			X	
Stanley and Beck, 2003	DSM-IV							X	

[a]Role functioning was assessed using instruments that measured: social, family and occupational and/or overall role functioning. Role functioning outcomes were frequently based on the Sheehan Disability Scale (SDS; Sheehan et al., 1996). The SDS assesses occupational, social, and family role functioning with three single-item scales. SDS scores can range from 0 to 10, with higher scores indicating worse role functioning (Sheehan, 2000). SDS scores can be summed in to a measure of overall role impairment.

[b]QOL was assessed using instruments that measured a person's subjective perceptions about one or more of the following areas: physical health status, mental health status, general well-being, and satisfaction with various aspects of daily life.

[c]Costs included direct costs related to use of health care resources and indirect costs related to lost work productivity/absenteeism.

[d]The number of days in the past month in which normal activities could not be performed or were limited because of symptoms.

[e]QOL assessment was commonly based on the SF-36 (Ware and Sherburne, 1992) or one of its briefer counterparts (Stewart et al., 1988; Ware et al., 1996).

role functioning, QOL, and economic outcomes. One common method was to examine disorder-specific outcomes in different subgroups. Common diagnostic subgroups comprised persons with a "pure," "single," or "comorbid" disorder. Table 3 shows how these subgroups were defined and are used to describe the burden of GAD in this review. Reporting outcomes associated with a "pure" or "single" disorder separately from those with a "comorbid" disorder was one method used to examine whether or not a particular disorder was uniquely impairing (i.e., whether or not impairments were due to the disorder itself as opposed

TABLE 2. Description of the Medical Outcomes Study 36- item Short Form Health Survey (SF-36)[a]

Scale Name	Description[b]
Physical functioning	Limitations in physical activities because of health problems
Role-physical	Limitations in usual role activities because of physical health problems
General health	Perceived general health status
Bodily pain	Amount of bodily pain and any limitations that result from it
Mental health	Psychological distress and well-being
Vitality	Energy and fatigue
Role-emotional	Limitations in usual role activities because of emotional difficulties
Social functioning	Limitations in social activities because of physical or emotional difficulties
Physical component summary (PCS)[b]	An empirically derived summary scale based on scores from the four scales assessing physical domains
Mental component summary (PCS)[b]	An empirically derived summary scale based on scores from the four scales assessing mental health domains

[a]Ware and Sherbourne, 1992 p. 473.
[b]Scale scores range from 0–100; higher scores represent better functioning.
[c]Summary scores have a mean of 50 and a standard deviation of 10 in a representative US population in 1998. Summary scales were not consistently used in analysis of SF-36 data.

TABLE 3. Description of diagnostic subgroups used to examine outcomes

Diagnostic subgroup	Description
Single GAD	GAD with no other comorbid disorder under study
Pure GAD	GAD with no MDD
Comorbid GAD	GAD with at least one other comorbid mental disorder under study
Pure MDD	MDD with no GAD

GAD, generalized anxiety disorder; MDD major depressive disorder.

to the disorder(s) that co-occurred with it). Several studies compared impairments among persons with GAD and subthreshold GAD. Persons with subthreshold GAD either do not meet the temporal or severity components required for diagnosis. Descriptions of impairments among those with subthreshold GAD are not included in this review.

RESULTS

GENERAL POPULATION STUDIES EXAMINING ROLE AND/OR QOL IMPAIRMENTS OF GAD

A total of 12 studies examined role functioning and/or QOL among persons with GAD in the general population (Table 1). These studies used nationally representative data from Australia [Andrews et al., 2001], Canada [Offord et al., 1996], Germany [Wittchen et al., 1998], the Netherlands [Bijl et al., 1998], Norway (National Population Register in Oslo), and the US [Kessler et al., 1994, 1997].

The extent to which role impairments of GAD were independent from MDD was examined in a nationally representative US sample [Kessler et al., 1999, 2002; Wittchen et al., 1994]. Analyses were based on current, past-year, and lifetime DSM-III-R disorders. Respondents with comorbid GAD/MDD were more likely than other respondents to describe impairments in role functioning. However, respondents with "pure GAD" and "pure MDD" were more likely to report role impairments than those with neither disorder [Kessler et al., 1999, 2002; Wittchen et al., 1994]. For example, a study of current disorders showed that ~63% of respondents with comorbid GAD/MDD ($n = 35$) reported at least one impairment day in the past month compared with 5.9% of respondents with neither disorder ($n = 5554$); the corresponding proportion (35%) was the same for respondents with pure GAD ($n = 52$) and pure MDD ($n = 232$) [Kessler et al., 2002]. A study of past-year DSM-III-R disorders showed that 27% of respondents with comorbid GAD/MDD ($n = 99$) reported the highest level of social impairment on a measure of social functioning compared with 8.4% of respondents with neither disorder ($n = 5217$); the corresponding proportion was 24% and 23% for respondents with pure GAD ($n = 92$) and pure MDD ($n = 489$), respectively [Kessler et al., 1999]. A similar pattern was observed for respondents with lifetime GAD when comorbidity with other affective disorders was examined [Judd et al., 1998].

Studies of both current and past-year disorders showed that role impairments of pure GAD were comparable in magnitude to those of pure MDD [Kessler et al., 1999, 2002]. Findings were maintained after controlling for the effects that might be due to other mental disorders and sociodemographic factors [Kessler et al., 1999, 2002]. To illustrate, findings for current disorders are described [Kessler

et al., 2002]. Pure GAD was associated with an average of between 1.5 and 5.4 impairment days in the past month, after adjusting for the presence of other mental disorders and sociodemographic characteristics. The independent incremental effects of GAD among persons who also had MDD were similar in magnitude (2.6 to 4.7 days) to those of MDD in persons who also had GAD. Past-month's role impairment of GAD was in the range previously observed for chronic medical conditions such as ulcers, arthritis, diabetes, and autoimmune disease [Kessler et al., 2001]. Moreover, in persons with comorbid GAD/MDD, GAD significantly contributed to role impairments over and above that which could be explained by MDD alone.

The extent to which QOL impairments of DSM-III-R GAD were independent of DSM-III-R MDD (and vice versa) was examined in a nationally representative Canadian sample [Stein and Heimberg, 2004]. This study examined associations between QOL, GAD, and MDD, adjusting for each along with lifetime dysthymia, age, gender, and social class. Disorders were based on DSM-III-R criteria. QOL outcomes were based on the Well-being scale [McDowell and Newell, 1987] and a series of five questions about satisfaction in different life domains (main activity, family relationships, friendships, leisure activities, and income). Well-being outcomes were examined from both a past-year and lifetime perspective. Dissatisfaction outcomes were examined exclusively from a lifetime perspective.

GAD respondents were significantly more likely than those without the disorder to report poor overall well-being, both in the past year and at some time in life (adjusted odds ratio [OR] 4.86, 95% confidence interval [CI]: 1.92–12.34; OR 4.06, 95% CI:2.80–5.89, respectively). GAD respondents were also significantly more likely than those without the disorder to report dissatisfaction with one's main activity and one's family life (adjusted OR 5.15, 95% CI: 2.04–12.97; OR 5.64, 95% CI: 2.35–13.51, respectively). MDD respondents were significantly more likely than those without the disorder to report poor well-being and dissatisfaction on all outcomes considered (adjusted ORs ranged from 2.01 [dissatisfaction with income] to 11.32 [overall well-being in the past year]). Findings for past-year GAD in the current study were similar to those found for GAD in a nationally representative Norwegian sample [Cramer et al., 2005].

Associations between 15 mental disorders and QOL and role functioning outcomes were examined in a nationally representative Dutch sample ($n = 7147$) [Bijl and Ravelli, 2000]. Analyses were based on DSM-III-R disorders in the past year. QOL outcomes were based on the SF-36 (Table 2). Respondents with single GAD ($n = 31$) reported mean SF-36 scores ranging from 58.9 (Vitality) to 90.8 (Physical Functioning). Compared with respondents with no mental disorder ($n = 5446$), single GAD respondents had significantly lower mean scores on two scales: Vitality (73.8 vs. 58.9) and Role-Emotional (95.4 vs. 76.5) (P's $< .001$). Associations between GAD and impaired vitality and emotional role functioning were maintained after controlling for sociodemographic characteristics, history of abuse or neglect before age 16, and the presence of a somatic disorder (adjusted βs of 0.16 and 0.21 for Vitality and Role Emotional, respectively; P's $< .001$). Respondents with single GAD showed a nonsignificant trend toward a greater number of days in the past month when normal activities were limited because of symptoms than respondents with no mental disorder ($M = 11.8$ and 1.1, respectively). However, GAD significantly predicted disability days after adjusting for the potential confounding characteristics described above (adjusted $\beta = -0.22$, $P < .001$).

Of the disorders under study, GAD, MDD, and dysthymia showed the strongest independent associations with Vitality, Role-Emotional, and disability days (adjusted βs ranging from 0.16 [GAD and Vitality] to −0.22 [disability days and all three single disorders], P's $< .001$). Overall, GAD was less impairing than mood disorders. In contrast, GAD was more impairing than other anxiety disorders (agoraphobia, social phobia, simple phobia and obsessive-compulsive disorder [OCD], and panic disorder [PD]), substance use disorders (alcohol/drug abuse and dependence), schizophrenia, and bulimia nervosa. Investigators noted that findings for schizophrenia and bulimia nervosa should be interpreted cautiously because there were very few cases (single schizophrenia [$n = 4$] and single bulimia nervosa [$n = 8$]; n's were not reported for total cases within the particular disorder groups).

The differential impact of GAD and/or MDD on role and QOL outcomes was examined in a nationally representative German sample ($n = 4181$) [Wittchen et al., 2000]. Analysis was based on DSM-IV disorders in the past year. As in previous studies [Kessler et al., 1999, 2002; Wittchen et al., 1994], impairments were examined among four mutually exclusive groups: pure GAD, pure MDD, comorbid GAD/MDD, and neither GAD nor MDD. Role impairment outcomes are presented in Table 4. Across all measures, comorbid GAD/MDD respondents were more likely than other respondents to report impaired role functioning. Notably, pure GAD respondents were more likely to report impaired role functioning than pure MDD respondents.

QOL outcomes assessed by the SF-36 were also reported separately for the four study groups (Table 5). Respondents with GAD and/or MDD reported significantly lower mean scores on all eight SF-36 scales compared with those with neither disorder. In general, GAD was associated with worse QOL outcomes than MDD. Pure GAD respondents showed significantly lower scores on General Health, Mental Health, Role-Emotional, and Vitality scales than respondents with pure MDD. Comorbid GAD/MDD respondents showed significantly lower scores on General Health, Mental Health, Social Functioning, and Vitality scales

TABLE 4. Outcomes of the impairment measures for 12-month generalized anxiety disorder (GAD) and major depressive disorder (MDD) in a representative German sample[a]

Impairment measure	Pure GAD $N=33$			Pure MDD $N=344$			GAD/MDD $N=40$			Neither GAD nor MDD $N=3764$		
	N	%W	95% CI	*N*	%W	95% CI	*N*	%W	95% CI	*N*	%W	95% CI
Self-perceived health												
Excellent or very good	3	10.1	3.1–27.9	34	12.4	8.7–17.3	0	0.0	—	792	23.5	21.9–25.1
Good	14	43.1	26.4–61.5	202	56.2	50.2–62.0	20	48.6	32.4–65.2	2343	62.9	61.1–64.7
Fair	16	46.9	29.6–64.9	108	31.5	26.2–37.2	19	51.4	34.9–67.6	571	13.6	12.5–14.8
Past month days impaired												
0	15	47.5	30.1–65.5	228	68.5	62.8–73.7	16	42.2	26.8–59.2	3463	93.3	92.5–94.1
1–2	1	2.1	0.3–13.4	17	4.4	2.6–7.2	3	6.3	2.0–18.4	120	2.7	2.2–3.2
3–5	4	16.2	6.2–36.3	24	6.4	4.2–9.7	2	3.9	1.0–14.5	95	2.2	1.7–2.7
6 or more	13	34.3	19.6–52.7	75	20.8	16.4–26.0	19	47.6	31.7–64.1	86	1.9	1.5–2.3
Past month's overall activity reduction[b]												
0	15	47.5	30.1–65.5	228	68.5	62.8–73.7	16	42.2	26.8–59.2	3463	93.3	92.5–94.1
0–9%	5	18.3	7.6–37.8	40	10.4	7.5–14.3	5	10.2	4.2–22.9	212	4.7	4.1–5.5
10–19%	4	5.5	2.0–14.5	16	4.2	2.5–7.1	6	13.7	6.2–27.8	37	0.8	0.6–1.2
20–29%	3	9.9	2.9–28.4	15	5.2	2.9–9.1	1	2.8	0.4–17.4	22	0.5	0.3–0.8
30–49%	3	7.9	2.5–22.7	16	3.9	2.3–6.5	2	8.0	2.0–27.3	11	0.3	0.1–0.5
≥50%	3	10.9	3.6–29.0	29	7.9	5.2–11.7	10	23.2	12.1–39.8	19	0.4	0.2–0.6

[a]Data are from the German National Health Interview and Examination Survey-Mental Health Supplement (GHS) (Wittchen et al., 1989).
[b]Based on number of days limited or lost due to symptoms and calculated as a past month overall work productivity reduction percentile.
Wittchen HU, Carter RM, Pfister H, Montgomery SA, Kessler RC. 2000. Disabilities and quality of life in pure and comorbid generalized anxiety disorder and major depression in a national survey. International Clinical Pharmacology 15:319–328. Copyright 2000 Lippincott, Williams and Wilkins. Adapted by permission.

TABLE 5. SF-36 scores associated with 12-month generalized anxiety disorder (GAD) and/or major depressive disorder (MDD) in a nationally representative German sample[a]

SF-36 scale	Pure GAD $N=33$		Pure MDD $N=344$		GAD/MDD $N=40$		Neither GAD nor MDD $N=3764$	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
General health	46.58[b,c]	38.9–54.3	59.10[b,d]	57.0–61.2	46.99[b]	40.8–53.2	68.39	67.8–69.0
Physical functioning	74.22[b]	64.6–83.8	82.96[b]	80.7–85.2	76.96[b]	69.2–84.7	88.37	87.7–89.0
Role physical	65.86[b]	51.5–80.2	72.23[b]	67.8–76.7	60.72[b]	45.3–76.1	85.48	84.4–86.5
Bodily pain	52.70[b]	43.6–61.8	56.33[b]	53.3–59.4	49.51[b]	41.8–57.2	69.07	68.2–70.0
Mental health	44.80[b,c]	39.7–49.9	56.60[b,d]	54.5–58.7	42.93[b]	38.2–47.7	74.00	73.5–74.5
Social functioning	57.73[b]	48.3–67.1	70.12[b,d]	67.1–73.1	57.10[b]	49.3–64.9	88.27	87.7–88.90
Role emotional	48.04[b,c]	35.8–60.3	67.98[b]	63.3–72.6	55.11[b]	40.0–70.2	91.48	90.7–92.3
Vitality	34.44[b,c]	29.1–39.8	46.95[b,d]	44.8–49.1	36.21[b]	31.4–41.0	61.29	60.7–61.9
PCS[e]	46.40	42.2–50.6	47.49	46.4–48.5	45.20	41.2–49.2	49.38	49.1–49.7
MCS[e]	33.64[b,c]	30.7–36.6	41.55[b,d]	40.2–42.9	35.11[b]	31.4–38.8	51.48	51.2–51.7

[a]Data are from the GHS. Some scores contain missing data. All scores, except the sum scores, are standardized to 0-100; higher scores indicate better QOL.
[b]Mean is significantly different from the mean in the "neither GAD nor MCD group"; $P<0.05$.
[c]Mean is significantly different from the mean in the "pure MDD" group; $P<0.05$.
[d]Mean is significantly different from the mean in the "GAD and MCD" group; $P<0.05$.
[e]Summary scores are z-transformed using a standardized US population, i.e., mean of 50 and a standard deviation of 10.
Wittchen HU, Carter RM, Pfister H, Montgomery SA, Kessler RC. 2000. Disabilities and quality of life in pure and comorbid generalized anxiety disorder and major depression in a national survey. International Clinical Pharmacology 15:319–328. Copyright 2000 Lippincott, Williams and Wilkins. Adapted by permission.

than pure MDD respondents. No significant differences in SF-36 scale scores were observed between respondents with comorbid GAD/MDD and pure GAD. Respondents with GAD and/or MDD reported SF-36 Physical Component Summary (PCS) scores that were similar to those of respondents with neither disorder. In contrast, respondents with GAD and/or MDD showed significantly lower mean SF-36 Mental Component Summary (MCS) scores than those with neither disorder.

Associations between GAD and/or MDD and risks of impairment were examined further in analyses controlling for sociodemographics and psychiatric comorbidity (Table 6). Compared with respondents who had neither GAD nor MDD, respondents with GAD and/or MDD showed significantly increased risks for reporting fair or poor health, at least 6 impairment days in the past month, an overall activity reduction of at least 30%, and an impaired SF-36 MCS score (i.e., a score ≤ 40). In contrast, respondents with GAD and/or MDD were no more likely than those with neither disorder to show an increased risk of impairment on the SF-36 physical summary scale. Significant differences were not observed between any associations for pure GAD, pure MDD, and comorbid GAD/MDD.

The effect of GAD on a summary measure of mental health-related QOL (SF-12) [Ware et al., 1996] was examined in a nationally representative Australian sample [Andrews et al., 2000; Hunt et al., 2004; Sanderson and Andrews, 2002]. Mean SF-12 MCS scores were reported for respondents with current DSM-IV GAD and current ICD-10 GAD, both with and without psychiatric comorbidity (Table 7). These SF-12 MCS scores fell more than one standard deviation below the population average of 50. Mean SF-12 MCS scores in the present study were similar to mean SF-36 MCS scores reported by German respondents with pure GAD ($M = 33.64$) and comorbid GAD/MDD ($M = 35.11$) [Wittchen et al., 2000; see Table 5 in this article].

Mean SF-12 MCS scores reported by respondents with DSM-IV GAD were compared with those reported by respondents with other DSM-IV mental disorders. Higher SF-12 MCS scores indicate better mental health-related QOL. Single GAD respondents had a higher mean SF-12 MCS score than single MDD respondents (single MDD: $n = 152$, $M = 34.9$ [$SE = 0.90$]; $t = -2.1$, $P < .05$) [Hunt et al., 2004]. Single GAD respondents did not differ from single PD respondents with respect to mean SF-12 MCS scores (single PD: $n = 25$, $M = 44.7$ [$SE = 5.0$]; ($t = 1.1$, $P = .28$) [Hunt et al., 2004]. However, when associations were examined in multivariate analyses, impairment of GAD was comparable in magnitude to that of MDD, and greater in magnitude than that of PD [Sanderson and Andrews, 2002].

The extent to which 14 different DSM-IV disorders uniquely impacted SF-12 MCS scores was examined in multivariate regression analysis [Sanderson and Andrews, 2002]. Regression analysis was used to predict differences in SF-12 MCS scores between respondents with a particular disorder and those who did not have the disorder. Predicted difference scores were adjusted for sociodemographic characteristics, the presence of a physical disorder, and psychiatric comorbidity. By comparing predicted difference scores associated with each disorder, it was possible to compare how SF-12 MCS outcomes for GAD compared with those of the other 13 disorders under study. GAD and mild, moderate, and severe depression were the only disorders to demonstrate a strong independent association with SF-12 MCS impairment (predicted difference scores compared with those without the disorder were -10.02 [$SE = 1.00$], -14.02 [$SE = 0.97$], -13.79 [$SE = 1.32$], and -14.76 [$SE = 1.15$] for GAD,

TABLE 6. Conditional associations of generalized anxiety disorder (GAD) and major depressive disorder (MDD) with health status and psychosocial impairments in a representative German sample[a]

	Pure GAD $N = 33$		Pure MDD $N = 344$		GAD/MDD $N = 40$	
	OR	95% CI	OR	95% CI	OR	95% CI
Perceived health: fair or poor	4.38	1.93–9.97	2.63	1.93–3.59	2.69	1.19–6.08
Past month's days impaired: 6 or more	13.87	5.14–37.40	9.52	6.19–14.65	21.05	8.92–49.66
Overall activity reduction $\geq 30\%$	20.48	6.62–63.40	15.99	8.83–8.94	30.90	11.81–80.86
SF–36 PCS score ≤ 40[b]	1.15	0.39–3.35	0.78	0.51–1.18	0.67	0.20–2.21
SF-36 MCS score ≤ 40	22.33	4.03–123.77	4.18	2.86–6.12	5.95	2.25–15.78

[a]Data are from the GHS; OR = odds ratio; comparison group: no 12-month GAD and no 12-month MDD. Controlled for age, gender and other psychopathology. OR, odds ratio; CI, confidence interval.

[b]≤ 40 is worse than approximately 84% of a representative US population.

Wittchen HU, Carter RM, Pfister H, Montgomery SA, Kessler RC. 2000. Disabilities and quality of life in pure and comorbid generalized anxiety disorder and major depression in a national survey. International Clinical Pharmacology 15:319–328. Copyright 2000 Lippincott, Williams and Wilkins. Adapted by permission.

TABLE 7. Mean SF-12 MCS scores for respondents with current generalized anxiety disorder (GAD), with and without psychiatric comorbidity[a]

Reference	GAD Sample	*N*	Mean SF-12 MCS Score
Sanderson and Andrews, 2002	DSM-IV	335	33.9 (0.90)[b]
Hunt et al., 2004	DSM-IV single GAD	100	38.8 (1.5)[b]
Andrews et al., 2002	ICD-10 GAD	251	36.4 (10.9)[c]
Andrews et al., 2002	ICD-10 Core GAD[d]	118	38.7 (10.2)[c]

[a]Data source: Australian National Survey of Mental Health and Wellbeing (Andrews et al., 2001).
[b](SE).
[c](SD).
[d]GAD identified as the "main or only" complaint in the previous one-month period.

MDD, and dysthymia, respectively; *P*'s $<.001$). PD, agoraphobia, and alcohol dependence showed moderate independent associations with impairment (predicted difference scores of -5.02 [$SE = 1.80$], -3.39 [$SE = 1.18$], and -2.22 [$SE = 0.74$], respectively; *P*'s $<.01$). Social phobia and drug dependence showed a mild independent association with impairment (predicted difference scores of -2.62 [$SE = 1.16$] and -2.87 [$SE = 1.26$], respectively; *P*'s $<.05$).

The Australian data were also used to examine the extent to which GAD was uniquely associated with role impairments [Hunt et al., 2004]. Multivariate analysis was used to examine whether GAD predicted role impairment beyond that which could be explained by MDD. GAD was significantly associated with an increased risk for having at least one role impairment day in the previous month (Wald $\chi^2 = 534.37$, $P<.001$). GAD was also associated with a significantly increased risk for showing moderate to severe impairment (BDQ; Wald $\chi^2 = 91.69$, $P<.001$) on the role functioning scale of the Brief Disability Questionnaire (BDQ) [Ormel et al., 1994; VonKorff et al., 1996]. These findings were maintained after controlling for MDD (Wald χ^2: 175.91 [impaired days]; Wald χ^2 36.99 [impaired BDQ]). Additional analysis showed that single GAD respondents reported a significantly higher mean number of impairment days than the single PD respondents (single GAD: $n = 100$, $M = 6.2$ days [$SE = 1.1$]; single PD: $n = 25$, $M = 2.5$ days [$SE = 1.0$]; $t = -2.8$, $P<.01$). Single GAD respondents did not differ significantly from single PD respondents in terms of mean impairment days (single MDD: $n = 142$, $M = 9.1$; $t = 1.8$, $P = .07$).

National Comorbidity Survey-Replication (NCS-R) data were used to evaluate the relative severity of several different past-year DSM-IV mental disorders in a nationally representative US sample ($n = 9282$ in the total part I sample) [Kessler et al., 2005b]. Severity was defined in terms of three mutually exclusive categories: mild, moderate, and serious. Severity categories were based, in part, on levels of role impairment assessed by the SDS and past-year's impairment days. Severity levels were also based on particular disorder-specific criteria. Notably, anxiety-specific criteria were not used to define the disability categories. Of the total part 1 sample ($n = 9282$), 3.1% were diagnosed with GAD. Severity ratings of mild, moderate, and serious were observed in 23.1%, 44.6%, and 32.3% of those with GAD, respectively.

In sum, general population studies are constrained by self-report and recall bias. However, use of general population data to examine role and QOL impairments of mental disorders offered at least two major advantages. First, analyses were based on large, representative national data sets. Second, study samples were not biased by help-seeking. Despite differences in methodologies, general population studies from around the world showed a consistent finding: GAD was uniquely associated with substantial impairments in role functioning and QOL. Although persons with GAD were more impaired when they had a comorbid disorder, persons with single and pure GAD were substantially more impaired than those without the disorder. Direct comparisons showed that role impairments of pure GAD were comparable in magnitude to those of pure MDD and in the range of those previously reported for chronic physical disorders. Impairments of GAD were at least comparable in magnitude to those of PD. Studies of DSM-IV disorders showed that QOL impairments of GAD were at least comparable in magnitude to those of MDD; studies of DSM-III-R disorders showed the opposite pattern. GAD appeared to have particularly strong negative associations with vitality, role functioning due to emotional difficulties, and overall well-being.

PRIMARY CARE STUDIES EXAMINING ROLE AND/OR QOL IMPAIRMENTS OF GAD

A total of nine primary care studies evaluated role functioning and/or QOL among patients with GAD (Table 1). Similar to studies of GAD in the community, primary care studies examined the extent to which impairments of GAD were independent of MDD and other mental disorders. QOL and role impairments of GAD were also compared with those of other mental and physical disorders.

Role functioning was examined in primary care patients in two separate US primary care settings

[Olfson et al., 1997, 2000]. The focus of these methodologically similar studies was to examine the extent to which DSM-IV GAD and other DSM-IV disorders were uniquely associated with role impairments in work, family, and overall functioning. The first study [Olfson et al., 1997] included a total sample of 1001 randomly selected patients with scheduled primary care appointments at a health maintenance organization. Of the 37 patients diagnosed with GAD, only four had single GAD. In this study, GAD was not uniquely associated with impairments on any of the three outcome measures considered. Notably, findings were not replicated when similar methods were used in the second study that included a larger sample of patients with single GAD [Olfson et al., 2000].

The second study [Olfson et al., 2000] included a total sample of 1007 consecutive patients with scheduled appointments at an urban general medical practice. The practice was affiliated with a public hospital that serves predominantly low-income and uninsured patients. Bivariate analysis was used to compare role impairments across three groups: single GAD ($n = 34$), comorbid GAD ($n = 115$), and no mental disorder ($n = 697$). Patients with GAD, as both a single and comorbid disorder, were significantly more likely than patients with no mental disorder to report missing at least 1 day of work in the past month due to symptoms (44.1% and 68.0% vs. 32.5%, respectively; P's $< .001$). Patients with GAD, as both a single and comorbid disorder, were also more likely than patients with no mental disorder to report worse overall family/social role functioning as assessed by mean 2-scale SDS scores. Two-scale SDS scores have a theoretical range between 0–20, with higher scores indicating worse overall family/social role functioning. Mean 2-scale SDS scores were 4.9 ($SD = 6.3$), 10.1 ($SD = 7.5$), and 1.7 ($SD = 3.8$) for patients with comorbid GAD, single GAD, and no mental disorder, respectively; P's $< .001$ (corresponding medians were 2, 10 and 0, respectively). Comorbid GAD patients, but not single GAD patients, were significantly more likely to describe family role functioning impairment than patients with no mental disorder (26.1% vs. 17.6% and 6.2%, respectively; $P < .001$).

Independent associations between disorders and role impairments were examined further in multivariate regression analyses, controlling for sociodemographic factors and psychiatric comorbidity. GAD was independently associated with a 2.2-fold (95% CI: 4.6–6.8) increased risk of work loss in the past month, a 3.0-fold (95% CI: 1.8–5.0) increased risk of family role impairment, and an expected increase of 5.5 points (95% CI, 4.6–6.8) on the 2-scale SDS. The expected increase on the 2-scale SDS for GAD was roughly equivalent to the 5.8 expected increases observed for MDD (95% CI: 5.0–6.7) and PD (95% CI: 4.6–6.9).

The Generalized Anxiety and Depression in Primary Care (GAD-P) study was a 1-day survey of ~20,000 consecutive patients and 558 primary care physicians in Germany [Wittchen et al., 2002]. This study examined associations between DSM-IV GAD and/or DSM-IV major depressive episode (MDE) and occupational role impairment. Occupational role impairment was defined as being unable to work at least 1 day in the past month because of symptoms. The study was unique in that it examined disorder-specific occupational role impairment outcomes due to physical symptoms separately from those due to psychiatric symptoms. Table 8 shows rates of occupational role impairment reported by primary care patients with GAD and/or MDE. Patients with GAD and/or MDE described significantly greater occupational role impairment due to physical and psychiatric symptoms compared with patients with neither disorder. Occupational role

TABLE 8. Rates of occupational impairment in the past month reported by primary care patients with generalized anxiety disorder (GAD) and/or major depressive episode (MDE)[a]

	No GAD/No MDE	Pure GAD		Comorbid GAD/MDE		Pure MDE	
Disability/role impairment	%	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
Disabled because of somatic problems	23.8	47.3	2.9 (2.4–3.4)	57.1	4.3 (3.3–5.7)	51.4	3.4 (2.9–4.0)
Disabled because of psychiatric problems	16.9	66.7	9.9 (8.3–11.7)	81.1	20.9 (14.8–29.0)	68.4	10.6 (8.9–12.7)

[a]Data are from the nationally representative German primary care study "Generalized Anxiety and Depression in Primary Care" (GAD-P) OR, odds ratio; CI, confidence interval.

Wittchen HU, Kessler RC, Beesdo K, Krause P, Höfler M, Hoyer J. 2002. Generalized anxiety and depression in primary care: prevalence, recognition and management. Journal of Clinical Psychiatry 63 (Suppl. 8) 24–32. Copyright 2002. Physicians Postgraduate Press. Adapted by permission.

impairment due to psychiatric symptoms was especially common. The mean number of past month's occupational role impairment days was substantial, with 9.9 for pure GAD (mean ratio [MR] compared with neither disorder of 1.4; 95% CI: 1.3–1.5); 15.3 for pure MDE (MR = 2.2; 95% CI: 2.1–2.4); and 16.5 for comorbid GAD/MDE (MR = 2.3; 95% CI: 2.1–2.5) [Wittchen et al., 2002:29].

The World Health Organization "Psychological Problems in General Health" (PPGH) was a standardized evaluation of 15 primary care sites in 14 countries. The PPGH included assessments of role functioning, based on the self-report BDQ [VonKorff et al., 1996] and the interview-administered Social Disability Schedule [Wiersma et al., 1988]. PPGH studies consistently found that a substantial proportion of GAD patients, both with and without comorbidity, reported marked impairments in role functioning [Maier et al., 2000; Ormel et al., 1994; Weiller et al., 1998]. For example, descriptive analysis of data pooled across all PPGH centers showed that GAD patients were approximately 5 times more likely to describe moderate/severe occupational dysfunction and moderate/severe physical disability than psychiatrically healthy controls (Table 9) [Ormel et al., 1994]. GAD patients also reported over three times as many impairment days in the past month as controls. In order to examine unique impairments associated with each of the disorders, analyses were repeated for patients with single disorders. As shown in Table 9, impairment in all single disorder groups was somewhat attenuated after excluding patients with comorbidity. Yet patients with single disorders showed substantially poorer role impairment outcomes compared with those without a mental disorder. The proportion (54%) of persons with single GAD describing moderate/severe

TABLE 9. Prevalence, psychiatric comorbidity, and disability by current ICD-10 diagnosis, pooled across 14 primary care centers in 15 countries (weighted estimates)

	Moderate or Severe, %		Mean	
	Occupational role dysfunction	Self-reported physical disability	*N* Disability days in past month	No. of Cases, Unweighted
Current ICD-10 diagnosis, all patients	7	12	1.7	1114
Psychiatrically well patients[a]				
ICD depressive episode	48	58	7.7	1174
ICD panic disorder	58	55	10.0	116
ICD agoraphobia	41	60	7.3	159
ICD neurasthenia	53	61	8.5	591
ICD hypochondriasis	39	44	4.7	66
ICD generalized anxiety	38	59	6.3	705
ICD alcohol dependence	32	31	5.1	206
ICD somatization disorder	38	58	6.3	232
Current ICD-10 diagnosis, patients with ≥2 psychiatric disorders are excluded	7	12	1.7	1114
Psychiatrically well patients[a]				
ICD depressive episode	39	46	6.1	438
ICD panic disorder	53	34	6.7	22
ICD agoraphobia	14	47	2.3	38
ICD neurasthenia	37	48	6.7	130
ICD hypochondriasis	42	45	6.3	25
ICD generalized anxiety	26	53	4.4	272
ICD alcohol dependence	20	18	4.2	83
ICD somatization disorder	21	42	2.6	53

[a]Well patients do not include patients with a definite or a subthreshold disorder or symptomatic patients.

Ormel J, Vonkorff M, Ustun B, Pini S, Korten A, Oldehinkel T. 1994. Common mental disorders and disability across cultures: results from the collaborative study on psychological problems in general health care. JAMA 272:1741–1748. Copyright 1994. American Medical Association. Reprinted by permission.

physical role impairment was higher than that for the other seven single disorder groups under study.

The extent to which untreated anxiety disorders and/or MDD impacted QOL was evaluated in a study of primary care patients enrolled in a health maintenance organization in the US [Schonfeld et al., 1997]. A total of 6703 eligible patients completed a screening assessment that included an anxiety and depression symptom inventory and the SF-36. Patients who were identified as having clinically significant anxiety symptoms and who had not received treatment for an emotional problem in the previous 6 months were administered a structured diagnostic interview. Of these anxious patients, 319 were identified as having at least one untreated DSM-III-R disorder, including: GAD ($n = 55$; $n = 14$ single cases); posttraumatic stress disorder (PTSD; $n = 110$; $n = 25$ single cases); simple phobia ($n = 94$; $n = 0$ single cases); social phobia ($n = 89$; $n = 23$ single cases); panic/agoraphobia ($n = 100$; $n = 20$ single cases); OCD ($n = 23$; 1 single case); and MDD ($n = 158$; $n = 54$). A total of 4242 eligible patients scored below anxiety cut-points and served as a nonanxious comparison group.

Regression analysis was used to estimate how the presence of five single disorders affected SF-36 scores predicted for a reference group of females age 25–34 with no mental disorders. For the reference group, predicted SF-36 scores were 91.9 (Physical Functioning), 83.6 (Social Functioning), 82.5 (Role-Physical), 84.0 (Role-Emotional), 75.6 (Mental Health), 59.9 (Vitality), 77.8 (Bodily Pain), and 77.5 (General Health). The presence of single GAD was estimated to significantly lower predicted scores for the reference group on six scales. Specifically, single GAD was estimated to lower predicted scores by approximately 14 points on Physical Functioning, 13 on Social Functioning, 21 on Role-Physical, 28 on Role-Emotional, and 16 on Vitality and General Health (P's $< .005$–$.05$). Compared to other single disorders, single GAD was estimated to have a significant impact on more QOL domains than social phobia and significantly fewer QOL domains than PD, PTSD, and MDD (significant reductions were observed on 6, 5, 7, and 8 predicted scale scores for single disorder groups GAD, social phobia, PD, and both PTSD and single MDD, respectively). Of all of the single disorder groups, single MDD was estimated to have the worst overall QOL outcomes. However, due to sampling design all patients with MDD also had clinically significant anxiety symptoms. Consequently, the extent to which MDD itself was responsible for poor outcomes is not clear. Findings are also limited by inclusion of only 14 cases of single GAD.

The study also examined how each specific disorder, when it occurred as part of a comorbid disorder, uniquely added to impairment on SF-36 scores. For these analyses, the reference group consisted of females age 25–34 who had multiple disorders (which accounted for the average impact of having more than one disorder on each predicted score). When occurring as part of a comorbid condition, GAD significantly added to impairment on predicted scores for Vitality and Physical Functioning scales. The presence of GAD, as part of a comorbid condition, was estimated to lower the predicted score of 45 (Vitality) and 87.3 (Physical Functioning) by 7.9 points and 6.5 points, respectively. Of all disorders occurring as part of a comorbid condition, GAD had the greatest negative impact on Vitality and the greatest negative impact next to PTSD on Physical Functioning.

The extent to which single GAD impacted SF-20 [Stewart et al., 1988] scores was examined as part of a primary care study in the US ($n = 1000$) [Spitzer et al., 1995]. This study used regression analysis to show the average difference in SF-20 scores between patients with 12 different disorders and patients with no mental disorder (most of whom had a physical disorder). Difference scores were adjusted for sociodemographics, site, and physical disorders. On all six SF-20 scales, single GAD was estimated to have significantly lower adjusted mean scores than respondents with no mental disorder. For patients with no mental disorder ($n = 614$), mean SF-20 scores were 77.8 (Physical Functioning), 66.2 (Bodily Pain), 84.4 (Role-Functioning), 80.8 (General Health), 67.0 (Social Functioning), and 65.3 (Mental Health). Compared with patients with no disorder, single GAD patients showed an average reduction in adjusted mean SF-20 scores of 21.8 on Physical Functioning, 24.1 on Bodily Pain, 43.6 on Role-Functioning, 28.5 on General Health, and 37.9 for Mental Health (P's $< .001$).

On all SF-20 scales, the 12 single disorder groups showed significant reductions in average adjusted mean scores compared with the reference group. Overall, single GAD was associated with adjusted mean score reductions that were typically about 30 points below that of the reference group (single GAD: $n = 70$; $M = 31$ for overall adjusted mean score reductions). The magnitude of impairment of single GAD was lower than the overall impairment of dysthymia ($n = 78$; $M = 35$); roughly comparable to the overall impairment of MDD ($n = 115$, $M = 32$), PD ($n = 36$; $M = 31$), and mutisomatoform disorder ($n = 82$; $M = 30$); and greater than overall impairment of anxiety disorder not otherwise specified (NOS) ($n = 90$; $M = 23$), minor depression ($n = 64$; $M = 20$), partial depression ($n = 63$; $M = 21$), hypochondriasis ($n = 22$; $M = 25$), somatoform disorder NOS ($n = 42$, $M = 21$), and binge eating ($n = 30$, $M = 27$).

A longitudinal primary care study examined associations between DSM-IV mental disorder groups and 1-year QOL outcomes [Jones et al., 2001]. Patients were randomly selected from primary care clinics at a

TABLE 10. Means (SD's) of the covariates, and modified SF-36 scale scores for primary care patients with generalized anxiety disorder (GAD), other Axis I diagnoses, and healthy controls[a]

	GAD ($N = 41$) *M* (*SD*)	Other Axis I diagnosis[b] ($N = 155$) *M* (*SD*)	No Axis I diagnosis ($N = 164$) *M* (*SD*)
Number of chronic illnesses	2.5 (1.6)[d]	2.6 (1.5)[d]	2.5 (1.4)[d]
Age	42.7 (11.5)[d]	42.9 (12.9)[d]	48.5 (14.7)[e]
Adjusted physical functioning[c]	51.6 (25.5)[d]	59.3 (25.8)[d]	66.6 (25.9)[e]
Adjusted role-physical[c]	32.7 (33.7)[d]	48.7 (34.2)[d]	63.2 (34.3)[f]
Adjusted role-emotional[c]	32.3 (25.8)[d]	44.8 (26.1)[d]	61.6 (26.2)[f]
Adjusted mental health[c]	49.2 (17.1)[d]	58.2 (17.4)[d]	71.1 (17.4)[f]

[a]Means in the same row with different superscripts d,e, and f are significantly different at $P < .05$.
[b]The other Axis I disorder group was predominantly comprised of patients with somatoform disorders ($n = 119$, 66%), other anxiety disorders ($n = 74$, 41%) and depressive disorders ($n = 50$, 27.8%).
[c]Values are adjusted for number of chronic illnesses and age.
Jones GN, Ames SC, Jeffries SK, Scardinci IC, Brantley PJ. 2001. Utilization of medical services and quality of life among low income patients with generalized anxiety disorder attending primary care clinics. International Psychiatry in Medicine 31:183–198. Copyright 2001 Baywood Publishing Company. Adapted by permission.

public hospital. QOL outcomes were based on modified SF-36 scale scores. In this study, four scales of the SF-36 were administered quarterly over a 1-year period. To characterize 1-year QOL outcomes, scale scores were calculated as the average of these four administrations. Resulting scales showed adequate reliability (Cronbach's alpha's > 0.74). Mean scores adjusted for age and number of chronic illness were compared across three patient groups: GAD, other Axis I disorders, and psychiatrically health controls. Modified SF-36 scores were adjusted for age and number of chronic illness (Table 10). Patients with GAD had significantly lower mean scores on Role-Physical, Role-Emotional, and Mental Health scales than the other two patient groups. GAD and other Axis I patients had significantly lower mean scores on the modified Physical Functioning scale than controls.

Studies in primary care are constrained by some potential limitations. Recruitment strategies may have resulted in increased sampling of frequent primary care attendees who might have been less healthy than other primary care patients. Two studies [Olfson et al., 2000; Wittchen et al., 2002] used self-report questionnaires to diagnose mental disorders, as opposed to structured diagnostic interviews. In one study, diagnoses of GAD and MDD generated by self-report instruments showed very good agreement with diagnoses generated by the Composite International Diagnostic Interview (GAD: kappa = 0.72; MDD: kappa = 0.76) [Krause et al., 2001; Wittchen et al., 2002]. Use of these reliable self-report diagnostic instruments enabled over 20,000 primary care patients to be screened for GAD and MDD in a single day [Wittchen et al., 2002]. In the second study [Olfson et al., 2000], a diagnosis of "any anxiety" generated by the self-report instrument showed good agreement with that of an independent mental health professional (kappa = 0.65) [Spitzer et al., 1999]; however, psychometric data specific to a diagnosis of GAD have not been published. Additional studies are needed to further examine the psychometric properties and the utility of these self-report diagnostic instruments.

Notwithstanding study limitations, GAD was found to be independently associated with substantial role and QOL impairments. Findings on the burden of GAD are largely consistent with findings from studies in the community. An additional notable finding was that GAD was identified as the most common anxiety disorder in primary care. The PPGH study ($n = 5446$) identified ICD-10 GAD as the most common anxiety disorder and the second most common mental disorder after MDD in primary care (point prevalence rates of 7.9% and 10.3%, respectively) [Ormel et al., 1994]. The GAD-P Study ($n = 20{,}245$) identified DSM-IV GAD as the most common anxiety disorder (point prevalence of 5.4%) [Wittchen et al., 2002]. Pure GAD was more common than comorbid GAD/MDD (point prevalence of 3.8% and 1.6%, respectively) [Wittchen et al., 2002]. This finding stands in contrast to studies of GAD in mental health settings where there is a very high rate of comorbidity [Massion et al., 1993]. The high prevalence and seriousness of GAD in primary care highlights the importance of GAD as a public health concern.

MENTAL HEALTH STUDIES EXAMINING ROLE AND/OR QOL IMPAIRMENTS OF GAD

Ten studies examined role functioning and/or QOL among persons who were seeking mental health treatment for GAD (Table 1). One study examined QOL in adult outpatients participating in a long-term naturalistic study [Massion et al., 1993]. In this study, the vast majority of study participants with GAD suffered from at least one comorbid mental disorder. Since study results were not adjusted for comorbidity,

the extent to which impairments observed in persons with GAD were due to the disorder itself could not be quantified. The remaining nine ($n = 9$) studies based assessment on patients who were either being screened or participating in a clinical trial (Table 1).

Two cross-sectional studies examined role functioning in patients seeking a new treatment for a DSM-III-R anxiety disorder [Kennedy et al., 2002; Mavissakalian and Zamar, 2000]. Both studies examined occupational, social, and family role functioning with the SDS before a new drug treatment was administered. The findings are presented in Table 11. In one study [Kennedy et al., 2002], SDS scores were compared across seven groups: six disorder groups (all without comorbidity) and psychiatrically healthy controls. Patients with single GAD showed moderate to severe impairments in work, social, and family role functioning. Patients with single GAD reported significantly higher SDS scores (indicating greater functional impairments) than those reported by patients with no mental disorder. Impairments in patients with single GAD were comparable in magnitude to those of patients in the other single disorder groups. The one exception was that GAD patients reported a significantly lower score on the family role functioning scale compared with patients with single MDD. Consistent with present findings, the second study [Mavissakalian and Zamar, 2000] found no differences in SDS scores between patients with GAD and patients with PD. Comparing findings for GAD patients across the two studies shows that GAD patients in the latter study [Mavissakalian and Zamar, 2000] reported SDS scale scores that were approximately one point higher than those in the former study [Kennedy et al., 2002]. Findings suggest a possible relationship between anxiety severity and functional outcomes. In the study where higher SDS scores were observed [Mavissakalian and Zamar, 2000], patients were required to show clinically significant levels of anxiety on the Hamilton Anxiety Rating Scale (HAM-A; [Hamilton, 1959]); there was no such eligibility requirement in the other study [Kennedy et al., 2002].

Two cross-sectional studies examined QOL among elderly patients seeking psychotherapy for anxiety symptoms [Diefenbach et al., 2003; Wetherell et al., 2004]. In one study [Wetherell et al., 2004], QOL was examined among 75 elderly patients with a principal diagnosis of DSM-IV GAD and 32 healthy controls. Pretreatment QOL was assessed with a modified SF-36; items assessing anxiety and depression were omitted from the scale to avoid redundancy with other measures included in the study. The six resulting scales showed adequate reliability (Cronbach's α's > 0.73). Table 12 presents modified SF-36 scale scores for patients in three groups: comorbid GAD, single GAD, and psychiatrically healthy controls. Findings suggested that comorbid GAD patients have significantly reduced QOL in the areas of role functioning due to physical and emotional problems, bodily pain, general pain, vitality, and social functioning compared with

TABLE 11. Work, social and family role impairments in two samples of patients seeking psychiatric treatment for a DSM-III-R anxiety disorder

		Sheehan Disability Scale (SDS)[a]		
Study reference Study groups	N	Work scale score Mean (SD)	Social scale score Mean (SD)	Family scale score Mean (SD)
Kennedy et al., 2002[b]				
GAD	65	3.97 (2.44)	4.41 (2.42)	4.40 (2.39)
Panic disorder (PD)	21	4.29 (2.10)	5.88 (2.09)	3.76 (2.67)
Social phobia	30	3.83 (2.10)	5.67 (2.54)	2.93 (2.26)
Obsessive compulsive disorder (OCD)	14	5.29 (2.16)	5.58 (2.83)	5.16 (2.61)
Mixed anxiety and depressive disorder	21	5.00 (2.41)	5.82 (2.32)	5.95 (1.94)
MDD	77	4.96 (2.46)	6.42 (2.21)	5.63 (2.04)
Comparison group	29	0.86 (0.99)	1.97 (2.14)	2.17 (2.18)
Mavissakalian and Zamar, 2000 p. 256				
GAD	46	5.3 (2.5)	5.6 (2.6)	5.2 (2.6)
Panic disorder	71	5.2 (2.8)	5.5 (2.7)	5.3 (2.7)

[a]SDS scale scores range from 0–10; higher scores indicate worse role functioning; scores ≥ 5 are associated with significant functional impairment (Sheehan, 2000).

[b]All diagnostic groups differed significantly from the comparison group in work and social disability scores. All disgnostic groups except PD and social phobia differed significantly from the comparison group in the family disability score. Social phobia was significantly different from MDD, OCD, and mixed anxiety disorder; PD was significantly different from MDD and mixed anxiety disorder; GAD was significantly different from MDD.

Kennedy BL, Schwab JJ. 2002. Work, social and family disabilities of subjects with anxiety and depression. Southern Medical Journal 95:1424–1427. Copyright 2002, Lippincott Williams & Wilkins. Adapted by permission.

TABLE 12. Modified SF-36 scale scores in older persons with and without GAD[a]

	Normals	Single GAD	Comorbid GAD			
SF-36 scales	*N* = 32 *M* (*SD*)	*N* = 36 *M* (*SD*)	*N* = 32 *M* (*SD*)	*F*	df	*P*
Physical functioning	74.2 (27.6)	61.3 (28.8)	63.3 (25.0)	2.07	2, 100	.13
Role physical	69.0 (40.5)[b]	45.6 (42.4)[b,c]	37.5 (37.6)[c]	5.29	2, 98	.007
Bodily pain	69.8 (26.1)[b]	56.6 (24.3)[b,c]	49.5 (21.0)[c]	6.31	2, 100	.003
General health	77.7 (17.8)[b]	56.6 (18.2)[c]	48.1 (20.2)[c]	22.40	2, 101	<.001
Vitality	70.0 (20.5)[b]	38.5 (19.5)[c]	36.9 (19.4)[c]	28.62	2, 101	<.001
Social functioning	86.7 (19.9)[b]	63.2 (22.8)[c]	53.9 (24.7)[c]	17.92	2, 99	<.001
Role emotional	91.1 (21.3)[b]	41.9 (35.6)[c]	37.6 (36.8)[c]	26.68	2, 101	<.001

[a]SF-36 items assessing anxiety and depression were omitted from the SF-36 to avoid duplication with other measures. Resulting scales showed adequate reliability (Cronbach's alphas >0.73). Letters (b,c) indicate significant pairwise difference, $P<.05$.
Wetherell JL, Thorp SR, Patterson TL, Golshan S, Jeste DV, Gatz M. 2004. Quality of life in geriatric generalized anxiety disorder: a preliminary investigation. Journal of Psychiatric Research 32:305–312. Copyright 2004, Elsevier Ltd. Adapted by permission.

those with no mental disorder. Findings also suggested that single GAD patients have significantly reduced QOL in the areas of general health, vitality, and social functioning compared with those without the disorder. No differences in QOL were observed between patients with comorbid GAD and single GAD.

Additional bivariate analyses were used to compare modified SF-36 scores between the total sample of patients with GAD and Medical Outcomes Study normative data [Ware, 1993]. Compared with normative data for patients with a recent myocardial infarction ($n = 107$), patients with GAD reported significantly more bodily pain, $t(165) = -5.54$, less vitality, $t(153) = -6.87$, worse social functioning, $t(138) = -7.51$, and more role functioning limitations due to emotional problems, $t(162) = -6.09$ (P's $< .001$) [Wetherell et al., 2004]. Compared with norms for patients with type II diabetes ($n = 541$), GAD patients described more role functioning limitations due to physical problems, $t(93) = -3.09$, more bodily pain, $t(100) = -5.3$, less vitality, $t(t98) = -7.37$, worse social functioning, $t(92) = -7.80$, and more role functioning limitations due to emotional problems, $t(94) = -8.05$ (P's $< .001$, except $P < .003$ for bodily pain) [Wetherell et al., 2004:308–309]. No differences were observed between patients with MDD ($n = 502$) and patients with GAD.

QOL was examined in a separate cross-sectional study of elderly patients [Diefenbach et al., 2003]. The sample included 30 elderly patients with DSM-IV GAD who were seeking psychotherapy and 21 healthy controls. Pretreatment QOL was assessed with the Quality of Life Inventory (QOLI) [Lehman, 2000]. The QOLI assesses the importance and the level of satisfaction associated with various life domains (i.e., health, work, recreation, relationships, home, self-esteem, and standard of living). GAD patients had significantly lower mean QOLI scores than healthy controls (0.87 [$SD = 1.96$] and 2.79 [$SD = 0.98$], $P < .05$, respectively). Mean QOLI scores were in the low range of impairment and the average range for GAD patients and healthy controls, respectively [Lehman, 2000].

Results from five clinical trials were used to characterize role and/or QOL impairments in help-seeking patients (Table 1). Across studies, patients described moderate/severe baseline impairments in role functioning and/or QOL. For example, patients ($n = 930$) from three separate clinical drug trials [Pollack et al., 2001; Rickels et al., 2003; Rosenthal, 2003] had a combined mean baseline SDS total score of 14.1; this score suggests moderate impairments in overall role functioning and is similar to scores reported for patients with untreated PD and MDD [Rickels et al., 2003; Sheehan et al., 1996]. One clinical drug trial [Allgulander et al., 2004] examined occupational impairment in employed subjects ($n = 208/566$); subjects showed substantial impairments in occupational role functioning ($M = 29.75$ on the Endicott Work Productivity scale, parts 1 and 2 [Endicott and Nee, 1997]). In addition, substantial QOL impairments were observed in the total sample ($n = 566$; $M = 63\%$ on the Quality of Life Enjoyment and Satisfaction Questionnaire [Endicott et al., 1993]). In a clinical trial of cognitive-behavioral therapy [Stanley et al., 2003], elderly patients ($n = 85$) also showed baseline QOL impairments on the Life Satisfaction Index [Wood et al., 1969] and on the QOLI [Lehman, 2000] ($M = 11.2$ and $M = 0.85$, respectively). In all of these studies, treatment groups that showed significant improvement on anxiety measures also showed significant improvement on validated role functioning and/or QOL measures.

Findings from clinical trials of GAD suggest a relationship between GAD (and its treatment) and QOL outcomes [Allgulander et al., 2004; Stanley et al., 2003]. Further evidence supporting this relationship was found when QOL scores were compared between

elderly patients who had significant improvements in anxiety treatment (responders) and those who did not (nonresponders), irrespective of treatment condition [Stanley et al., 2003:313]. Bivariate comparisons showed that responders had significantly higher (better) LSI-Z and the QOLI scores compared with nonresponders (LIS-Z: $t(63) = 3.5$, $P < .01$; QOLI: $t(63) = 3.21$, $P < .01$) [Stanley et al., 2003]. Mean scores suggested meaningful differences in QOL between responders and nonresponders were meaningful (QOLI: for responders, $M = 2.4$ [$SD = 1.71$], and for nonresponders, $M = 0.80$ [$SD = 1.68$]; LSI-Z: for responders, $M = 17.4$ [$SD = 4.36$], and for nonresponders, $M = 11.3$ [$SD = 6.85$]) [Stanley et al., 2003:313].

Findings from mental health studies are constrained by limitations. Patients in these studies were either being screened for eligibility or were participating in a clinical trial. Clinical trial participants with GAD were required to be physically healthy, and with one exception [Wetherell et al., 2004], to be free of psychiatric comorbidities. With two exceptions [Kennedy et al., 2002; Wetherell et al., 2004], eligible patients were also required to demonstrate clinically significant anxiety symptoms (i.e., HAM-A scores >18). Consequently, findings are subject to considerable selection bias and may not be generalizable to other more typical patients with GAD in mental health settings. Notwithstanding these limitations, these studies are useful in showing role and QOL impairments in persons who have been identified by a clinician as having clinically significant anxiety. These studies also showed that patients in clinical trials of GAD have similar baseline impairments as patients with MDD and PD. Clinical trial findings suggest that efficacious treatment of anxiety symptoms can translate into improved role functioning and QOL. However, these findings require confirmation in long-term studies in naturalistic settings.

ECONOMIC BURDEN OF GAD

Three studies reported on the economic burden of GAD (Table 1). Economic costs were estimated based on self-reports of health care resource use (direct costs) and impairment days (indirect costs due to lost work productivity and/or absenteeism). A cross-sectional retrospective study examined costs related to use of health care resources and lost work productivity (sick leave) in patients with DSM-III-R GAD in France [Souetre et al., 1994]. The time-frame of the study was the past 3 months. Costs were compared between GAD patients who symptoms of another mental and/or physical disorder (i.e., GAD with comorbidity; $n = 604$) and GAD patients without comorbidity ($n = 395$). The most prevalent medical comorbidities included self-reported gastroenterological symptoms (14.6%), gynecologic symptoms (9.8%), and cardiac symptoms (7.6%). The most prevalent psychiatric comorbidities included depressive symptoms (27%) and substance-related problems (25%).

Patient self-report data were collected on use of health care resources and lost work for the past 3 months. Unit costs were based on a variety of sources. Hospital costs were determined using the average "per diem" cost as assessed from a representative sample of French hospitals. Costs of diagnostic procedures and medical service use were determined using published data [Sociale, 1992] and official tariffs lists. Pharmaceutical costs were assessed using market prices, excluding taxes (VAT). Indirect work costs were derived using actual loss of income (salary). Although costs were based on French cost estimates, the results were reported in US dollars ($US, year not reported).

Three-month total costs of GAD were estimated to be $US 733 (no comorbidity) and $US 1208 (with comorbidity).[1] For GAD patients without comorbidity, 42%, 33%, 21%, 3%, and 2% of the total cost was associated with outpatient services, absenteeism from work (sick leave), hospitalization, medications, and diagnostic procedures, respectively. For GAD patients with comorbidity, 35%, 34%, 25%, and 3% of the total cost was associated with hospitalization, absenteeism from work, outpatient services, and both diagnostic procedures and medications, respectively. GAD patients with comorbidity were estimated to have significantly higher direct mean costs compared with GAD patients without comorbidity in the following sectors: hospitalizations ($423 vs. $158, $P < .01$); psychiatry ($187 vs. $55, $P < .05$); internal medicine ($131 vs. $35, $P < .05$); diagnostic procedures ($44 vs. $19, $P < .01$); and medications ($43 vs. $25, $P < .001$). Workplace costs due to absenteeism also differed significantly between GAD patients with comorbidity and GAD patients without comorbidity ($416 vs. $243, $P < .001$).

The total cost of anxiety disorders in the US in 1990 was examined using data from the NCS, supplemented with data from an HMO, national statistics, professional meetings, and periodicals and written communication from industry sources [Greenberg et al., 1999]. DSM-III-R anxiety disorders used to estimate the total cost of anxiety included GAD, PD, social phobia, simple phobia, agoraphobia, and PTSD. The total cost of anxiety disorders was estimated to be approximately $42.3 billion in 1990 in the US. The total cost estimate comprised five components: nonpsychiatric medical treatment costs (23.0 billion; 54% of the total cost); psychiatric treatment costs ($13.3 billion; 31%); indirect workplace costs ($4.1 billion; 10%); mortality costs ($1.2 billion; 3%); and prescription pharmaceutical costs ($0.8 billion; 2%).

[1]When the present costs were inflated and converted to Euros for 2003, costs were estimated to be €954 and €1633 for GAD patients without comorbidity and with comorbidity, respectively [Lothgren, 2004].

Costs were adjusted for the presence of other psychiatric disorders and sociodemographic characteristics.

Additional analyses examined the impact of individual disorders on selected direct costs (i.e., hospitalization, consultations with different types of mental health professionals, consultations with medical specialists such as cardiologists and gynecologists, and other types of professionals) and indirect costs (i.e., absenteeism and work cutback days) [Greenberg et al., 1999]. GAD was significantly associated with use of family doctors, medical specialists, and work cutback days. GAD ranked in the top four disorders associated with risk of service use and adverse workplace outcomes; PTSD, PD, agoraphobia, GAD, social phobia, and simple phobia significantly impacted on 8, 6, 4, 3, 1, and 0 service use/adverse workplace outcomes, respectively. It is notable that GAD did not significantly impact costs associated with use of any type of mental health professional under study. It is possible that the particular cost distribution for GAD partially results from inappropriate treatment of unrecognized GAD in medical settings.

An economic model was developed to estimate costs of brain disorders in Europe (25 EU member countries plus Iceland, Norway, and Switzerland) [Andlin-Sobocki et al., 2005]. Costs of five DSM-IV anxiety disorders were considered, including GAD, PD, social phobia, specific phobias, agoraphobia without panic, and OCD. Economic inputs for anxiety disorders were based on a cost-analysis of data on health care resource use and lost work productivity (based on sick leave) in a nationally representative German sample [Andlin-Sobocki and Wittchen, 2005]. Mean costs per case of anxiety disorder were calculated as excess costs compared with respondents without an anxiety disorder. In order to estimate costs of anxiety disorders across Europe, estimated costs (for Germany) were transformed to Euros for 2004, adjusted for purchasing power parity using national statistics and combined with prevalence for each European country. Therefore, the cost per case of anxiety disorder for each country is presented in terms of Euros in 2004 adjusted for purchasing power parity (€2004 PPP). Aggregated European cost estimates were also derived by summing the estimates for each country. No adjustments were made for comorbidity. The average cost per case of GAD in Europe was estimated to be €1804 in 2004, with country estimates ranging from €531 (Estonia) to €3238 (Switzerland). The estimated cost per case of GAD in Europe in 2004 was higher than that of the other anxiety disorders under study, with corresponding estimates of €350, €517, €937, €941, and €967 for OCD, specific phobia, social phobia, agoraphobia, and panic disorder, respectively.

Economic studies of GAD were limited by use of self-report data regarding service utilization and work outcomes. However, limited findings suggested that GAD imposes a substantial economic burden on the health care system and society in general.

DISCUSSION

This study reviewed a total of 34 studies on the burden of GAD (Table 1). Despite differences in methodologies, studies from around the world consistently showed that GAD was uniquely associated with substantial human and economic costs. Persons with GAD described difficulties due to both physical and emotional symptoms. GAD sufferers with a comorbid disorder reported role and QOL impairments of a higher magnitude than those who did not. Yet GAD suffers without comorbid MDD and/or another mental disorder were substantially more impaired than those without the disorder. For example, pure GAD was associated with an average of between 1.5 and 5.4 impairment days in the past month, after adjusting for the presence of other mental disorders and sociodemographic characteristics [Kessler et al., 2002]. The 30-day role impairment of pure GAD was comparable in magnitude to that of pure MDD [Kessler et al., 2002], and in the range previously reported for chronic medical conditions such as ulcers, arthritis, diabetes, and autoimmune disease [Kessler et al., 2001]. Primary care patients with pure GAD described significantly greater occupational role impairment due to physical and psychiatric symptoms compared with those with neither GAD nor MDD [Wittchen et al., 2002]. Moreover, persons with pure GAD reported significantly lower scores on all eight SF-36 scales compared with those without the disorder. The findings suggest that persons with GAD often experience significantly reduced QOL in the areas of general health, physical health, bodily pain, vitality, mental health, role functioning due to physical and emotional difficulties, and social functioning compared with those without the disorder. Findings were maintained after adjusting for the effects of comorbidity and sociodemographic characteristics [e.g., Wittchen et al., 2000]. There is provisional evidence that effective treatment of anxiety symptoms might translate into substantially improved role functioning and QOL. The high prevalence and seriousness of GAD highlight the importance of recognizing and treating the disorder, whether or not it is part of a comorbid condition.

Studies typically showed that role and QOL impairments of GAD were at least comparable in magnitude to those of other anxiety disorders, somatoform disorders, and physical conditions, and greater in magnitude than those of substance use disorders. Large representative studies showed that role impairments of pure GAD were similar in magnitude to those of pure MDD. Studies of DSM-IV disorders showed that QOL impairments of GAD were at least comparable in magnitude to those of MDD; studies of DSM-III-R disorders showed the opposite pattern. Divergent findings of the differential impact of GAD and MDD on outcomes might be due to differences in methods. For example, GAD is a chronic persistent disorder requiring symptoms to be present for at least

6 months for a diagnosis [APA, 1980, 1994; WHO, 1993]. In contrast, because MDD is frequently an episodic disorder, one might expect that a considerable proportion of affected persons may show substantial impairments only at the height of the episode. An episode of depression is defined by the presence of symptoms most of the time almost every day for a period of at least 2 weeks [APA, 1980, 1994]. When examining the differential impact of GAD and MDD from an epidemiological perspective, it was common to describe impairments associated with both disorders over the past 1-year period [e.g., Cramer et al., 2005; Kessler et al., 1999; Stein and Heimberg, 2004; Wittchen et al., 2000]. In contrast, clinical studies typically used a narrower cross-sectional time-frame of 4 weeks. In the latter case, the magnitude of impairment would be expected to be greater for MDD as compared with GAD.

GAD was associated with considerable economic costs. Economic costs were estimated based on self-reports of health care resource use (direct costs) and impairment days (indirect costs due to lost work productivity and/or absenteeism). Economic costs were higher for GAD suffers with comorbidity than those without comorbidity [Souetre et al., 1994]. The cost of brain disorders in the Europe study estimated the average cost-per-case of DSM-IV GAD to be €1804 in Europe in 2004, after adjusting for differences in purchasing power between countries; the estimated per-patient cost of GAD was higher than that of any of the other anxiety disorders considered [Andlin-Sobocki et al., 2005]. In a study estimating the total cost of anxiety disorders in the US in 1990, GAD was identified as a significant cost-driver with respect to use of family doctors, medical specialists (e.g., gynecologists and cardiologists), and work cutback days [Greenberg et al., 1999]. Notably, GAD did not significantly impact costs related to use of mental health services.

Findings on economic studies of GAD complement findings from other studies showing that GAD patients use primary care and gastroenterology services significantly more often than those without the disorder [Kennedy and Schwab, 1997; Wittchen et al., 2002]. For example, GAD patients were significantly more likely to visit primary care at least four times in the past year compared with those without the disorder [Wittchen et al., 2002]. Notably, primary care patients with GAD were far more likely to seek treatment for vague somatic illnesses, pain, and sleep disturbance than for anxiety [Wittchen et al., 2002]. GAD patients were also significantly more likely to consult gastroenterologists in the past year than persons with no mental disorder [Kennedy and Schwab, 1997]. The same study found that GAD patients were twice as likely to seek help from gastroenterologists as psychiatrists [Kennedy and Schwab, 1997]. GAD patients were also found to be high users of cardiology services, often for medically unexplained symptoms [Carter and Maddock, 1992; Kane et al., 1988; Louge et al., 1993; Wulsin et al., 1991]. It is possible that the particular cost distribution for GAD partially resulted from inappropriate treatment of unrecognized GAD in medical settings. Future studies are needed to understand more about the current economic burden of GAD. Studies are also needed to examine the potential "hidden" costs arising from high and inappropriate use of medical resources in patients with unrecognized GAD, and to examine whether or not costs differ significantly between GAD patients who have been recognized and effectively treated and those who have not.

GAD is associated with serious human and economic costs. Quality of care initiatives that have been employed to increase recognition and improve treatment outcomes of people with MDD should be extended to effective management of GAD.

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