Comorbidity in Primary Care: Presentation and Consequences

Hans-Ulrich Wittchen, Ph.D.; Roselind Lieb, Ph.D.;
Ursula Wunderlich, Ph.D.; and Peter Schuster, Dipl. Psych.

Comorbidity is a well-established phenomenon in depressive disorders, and it is widely agreed that the majority of depressive disorders examined in both primary care and the general population are not "pure." This article reviews comorbidity findings in general population and primary care surveys. The implications of comorbid depressive disorders are discussed in terms of their presentation and recognition in primary care, patterns of course and outcome, and associated impairments and disabilities. Data from a World Health Organization study, conducted in primary health clinics in 15 countries, demonstrate that 62% of all depressive cases also suffer from at least one other current mental disorder and that the primary reason for patient visits is rarely of a psychological nature, with the majority of attendees complaining primarily of somatic symptoms (41%), pains (37%), and fatigue and sleep problems (12%). Similar results are presented from 2 recent large representative population surveys, the National Comorbidity Survey and the Early Developmental Stages of Psychopathology Study. The implications of such comorbidity are viewed from various perspectives: the form of depressive presentations in primary care, the recognition of depression in health care, and health services utilization, impairments and disabilities, and course and outcome.
(J Clin Psychiatry 1999;60[suppl 7]:29–36)

Comorbidity, defined as "the presence of more than 1 specific disorder in a person in a defined period of time,"[1,2(p9)] is a well-established phenomenon in depressive disorders. Despite some variations due to the definition of comorbidity in terms of conceptual differences, coverage of diagnoses, time windows (lifetime versus current), assessment methods, and design and analyses, there is considerable agreement that the majority of depressive disorders examined in clinical samples (in both primary care and the general population) are not "pure."[2,3] Furthermore, there is some evidence across studies using diagnostic interviews according to operationalized classification systems (DSM-III[4] to DSM-IV[5]) that the frequency of comorbidity is most pronounced in specialized mental health services and slightly less frequent in general population samples.[6] There is presently no uniformly accepted, comprehensive, and coherent theoretical framework for comorbidity that allows integration of the many comorbidity findings. However, it has become evident that comorbidity in depressive disorders is not merely a random phenomenon or an artifact of the assessment strategy.[7,8] There is increasing evidence from a number of well-controlled studies that the concept of comorbidity is a useful approach, not only in the study of etiologic and pathogenic factors (vulnerability and risk factors), but also in its implications for course and outcome, seeking help and treatment, and associated patterns of impairments and disabilities.

This article reviews comorbidity findings in general population and primary care surveys. The implications of comorbid depressive disorders are discussed in their presentation and recognition in primary care, patterns of course and outcome, and associated impairments and disabilities.

FREQUENCY AND TYPES OF COMORBIDITY IN DEPRESSIVE DISORDERS

Common Comorbidities With Regard to Mental Disorders

Prevalence. Prevalence data have been collected from primary health clinics in 15 countries around the world as part of the World Health Organization (WHO) Collaborative Study "Psychological Problems in General Health Care." These data demonstrate that across participating centers and countries, 11.7% of all primary care attendees

From the Max Planck Institute for Psychiatry, Clinical Psychology and Epidemiology, Munich, Germany.

The International Consensus Group on Depression and Anxiety held the meeting "Focus on Primary Care Management of Depression," October 15–16, 1998, in Charleston, S.C. The Consensus Meeting was supported by an unrestricted educational grant from SmithKline Beecham Pharmaceuticals.

Reprint requests to: Hans-Ulrich Wittchen, Ph.D., Max Planck Institute for Psychiatry, Clinical Psychology and Epidemiology, Kraepelinstrasse 10, D-80804 Munich, Germany.

Table 1. Odds Ratios of Current Depression With Other Frequent Disorders[a]

Comorbid Condition	Odds Ratio (OR)	95% Confidence Interval (CI)
Physical disorder	1.1	0.9 to 1.3
Alcohol dependence[b]	2.1	1.6 to 2.8
Subthreshold anxiety	3.9	3.1 to 4.9
Anxiety disorders[c]	9.3	7.6 to 11.4
Other psychological disorder[d]	10.6	8.6 to 13.0

[a]Adapted from reference 8, with permission. For physical disorder, N = 5315; for remaining categories, N = 5447. Diagnoses given per ICD-10 criteria.
[b]Harmful use of alcohol (F10.1) or alcohol dependence (F10.2).
[c]Current generalized anxiety disorder (F41.1), panic (F41.0), or agoraphobia (F40.0).
[d]Neurasthenia (F46.0), somatization disorder (F45.0), hypochondriasis (F45.2), or dysthymia (F34).

Table 2. Comorbidity of Current 12 Months (DSM-III-R/DSM-IV) Major Depressive Disorder With Other Mental Disorders in the National Comorbidity Survey (NCS) and the Early Developmental Stages of Psychopathology Study (EDSP)[a]

	NCS			EDSP		
Other Diagnoses	%	OR	95% CI	%	OR	95% CI
Any anxiety disorder	51.2	4.2	3.4 to 8.6	48.6	3.3	2.4 to 4.1
Panic disorder	8.6	5.0	3.1 to 8.0	5.0	4.2	2.1 to 8.5
Generalized anxiety disorder	15.4	8.2	5.0 to 13.5	17.0	8.2	3.5 to 10.3
Agoraphobia	12.6	4.4	2.8 to 6.9	7.6	3.2	1.9 to 5.4
Social anxiety disorder	20.0	3.3	2.4 to 4.5	17.3	3.1	2.2 to 4.5
Simple phobia	23.7	3.7	2.8 to 4.8	30.0	2.6	2.0 to 3.5
Posttraumatic stress disorder	15.2	6.0	4.1 to 8.6	4.9	6.2	2.8 to 13.6
Obsessive-compulsive disorder	…			2.0	2.6	1.8 to 7.8
Separation anxiety disorder	…			1.5	2.6	0.8 to 7.8
Any substance use disorder	18.5	1.9	1.4 to 2.8	23.4	1.3	1.0 to 1.8
Alcohol dependence	13.0	2.0	1.3 to 3.0	8.0	1.2	0.7 to 2.0
Alcohol abuse	1.4	1.1	0.6 to 1.9	15.9	1.1	0.7 to 1.5
Drug abuse/dependence	7.5	3.1	2.0 to 4.6	7.8	2.3	1.4 to 3.8
Any somatoform disorder	…			23.5	2.5	1.8 to 3.4
Any eating disorder	…			6.9	2.8	1.6 to 5.1
Other disorders[b]	4.0	5.2	2.4 to 11.2	4.6	4.8	2.2 to 9.6

[a]Age range covered by NCS, 15–55 years; age range covered by EDSP, 14–24 years. Symbol: ... = not assessed.
[b]Other disorders include conduct disorder and dysthymia.

suffer from threshold ICD-10 depressive disorders at the time of contact.[9] Using the primary care version of the Composite International Diagnostic Interview,[9] 62% of all depressive cases were found to also suffer from at least one other current mental disorder. Most frequent co-occurring mental disorders (Table 1) were any anxiety disorders (generalized anxiety disorder, panic disorder, agoraphobia; odds ratio [OR] = 9.3), neurasthenia (OR = 6.2), hypochondriasis (OR = 6.1), somatization disorder (OR = 5.9), dysthymia (OR = 8.2), and alcohol dependence (OR = 2.1).

The finding that major depressive disorders rarely present in their pure form is consistent with results from

Table 3. Percentages of Lifetime Pure, Primary, and Secondary Major Depressive Disorders Among All Meeting Criteria in the NCS and the EDSP[a]

	NCS (Retrospective)			EDSP (Prospective)		
Subjects	Pure	Primary	Secondary	Pure	Primary	Secondary
Total	26.0	12.2	61.8	34.8	15.5	49.7
Women	30.1	12.2	57.7	31.5	13.5	55.1
Men	18.6	12.1	69.3	40.6	19.0	40.6

[a]Respondents with dysthymia and major depressive disorder were counted having as pure disorders. The EDSP uses a stricter temporal priority criterion, thus cases counted as secondary in the NCS would be counted as same year or primary in the NCS.

recent large representative population surveys. The National Comorbidity Survey (NCS)[10,11] and, with more complete coverage of diagnoses, the Early Developmental Stages of Psychopathology Study (EDSP)[12,13] found quite similar patterns and associations. In the NCS, only 26% of all depressive disorders occurred in their pure form, and in the EDSP this figure was 34.8%. Significant odds ratios were found for most specific anxiety and somatoform disorders and for substance abuse and dependence and eating disorders (Table 2).

Temporal relationship. Another consistent finding in both retrospective (NCS) and prospective (EDSP) longitudinal studies[14] is that the vast majority of comorbid depressive disorders occur secondary to another mental disorder (Table 3). Even though to date only a very limited range of disorders has been covered, commonly, comorbid major depression is temporally preceded by anxiety and somatoform disorders as well as substance abuse and eating disorders. It is also noteworthy that the temporal relationship seems to be stable in both retrospective (NCS) and prospective (EDSP) studies. The consistent temporality patterns have stimulated considerable research into the pathogenic role of primary anxiety and somatoform disorders as risk factors for both the onset and persistence of major depression. In this respect, findings by Kessler et al.[11] are particularly noteworthy. They demonstrated, using discrete-time survival modeling, remarkable diagnostic differences in patterns of temporality. Whereas primary phobia disorders usually precede onset of depression by many years, others, such as panic disorder, are associated with a fairly rapid onset of secondary depression. Generalized anxiety disorders were found to occur relatively frequently within the same year as depression.

Common Comorbidities With Regard to Somatic Disorders

Although a close association between specific somatic illnesses and depressive symptomatology has long been suggested, such an association with regard to full-blown major depression as a strictly defined diagnosis is a more recent finding. However, unlike mental disorder comorbidity, the meaning and the implications of such comorbidity patterns with somatic disorders are less well stud-

ied. Furthermore, few epidemiologic studies and limited data are available from primary care settings.

Endocrine disorders. Of the various hypothalamic-pituitary end organ axes, the thyroid and adrenal systems have been implicated most often in affective disorders. Patients with primary thyroid disease have high rates of depression, and patients with Addison disease or Cushing syndrome have relatively high rates of depressive and anxiety symptoms. Support for the link between endocrine axes and depression comes from many studies in which alterations in components of the thyroid and adrenal axes have been documented. All observed adrenal axis alterations in depression studies thus far are state-dependent, whereas the thyroid axis alterations may be partially trait and partially state markers.[15] Consistent with these associations, Sonino and Fava[16] conclude in a recent review that endocrine disorders are commonly associated with depressive disorders; however, to date, no clear conclusions can be drawn with regard to causality.

Acquired immunodeficiency syndrome. Significant associations between the infection produced by the human immunodeficiency virus (HIV) and major depression have been reported from a WHO multicenter study[17] and are consistent with several other studies.[18]

Cancer. Findings suggest, with some consistency, that certain types of cancer are associated with an increased risk of depression. Estimates range from 11% to 50%,[19] and risks were found to be especially frequent in pancreatic, breast, and cervical cancer. The psychological and neurobiological mechanisms behind this association are still open to debate; one particularly critical question is to what degree the observed increased comorbidity is due to the associated pain symptomatology and/or secondary side effects of pharmacologic treatments. Nevertheless, there are a number of findings that indicate depression comorbidity in cancer illnesses influences course and outcome.[20]

Cardiac diseases. A link between cardiac diseases and depression has recently received attention. There is slowly accumulating evidence that depression might pre dispose an individual toward cardiovascular and cerebrovascular diseases. Furthermore, patients experiencing depression following a myocardial infarction seem to have higher mortality than nondepressed patients.[21]

Epidemiologic studies. Epidemiologic studies reporting prevalence estimates of depression in the somatically ill (using standardized assessment instruments for mental disorders) are still sparse. Aside from the "landmark" Medical Outcomes Study[22] and limited information provided by the WHO study on primary care,[9] both documenting an increased risk of major depressive disorder for the chronically medically ill, few large-scale population-based studies are available. In this respect, the Groningen Longitudinal Aging Study[23] is noteworthy. The study population of 8723 persons aged 57 and over were enlisted with 27 general practitioners and rated for a wide range of specific chronic and acute medical conditions. Depression was assessed using the Hospital Anxiety and Depression Scale; the response rate was 62% (N = 5279).

In that study, Ormel and colleagues[23] demonstrated that among those with medical conditions, 21.0% (768/3655) fulfilled criteria for depression, whereas only 9.3% (151/1624) of those without medical conditions were found to be depressed. Thus, irrespective of the type of medical disorder, there is at least a 2-fold increase in depression among the medically ill. However, the strength of this association seems to be largely dependent on the type of disorder. A pilot study of the German National Morbidity Survey (NMS)[24] based on standardized diagnostic assessments of both somatic illnesses and mental disorders of a representative population sample aged 18 to 65 years, confirmed by and large the overall increased risk of medically ill patients to suffer from major depression. In accordance with the study by Ormel et al.,[23] the risk for depressive disorders was highest in chronic conditions as well as those associated with enduring pain.

Pain. The key role of pain in mediating a considerable proportion of the observed comorbidity between physical and depressive illnesses has recently been comprehensively explored by Von Korff and Simon,[25] who reviewed data from primary care attendees and other population-based studies. They summarize (1) that pain is strongly related to both anxiety and depression, (2) that characteristics that are most strongly associated with depression are the diffuseness of pain and the extent to which it interferes with activities, and (3) that when chronic pain precedes the onset of major depression, it is likely that the depression will follow a chronic course. The authors conclude that "pain constitutes a significant physical and psychological stressor that may induce or exacerbate psychological distress. Thus, pain and psychological illness ('depression') should be viewed as having reciprocal psychological and behavioral effects involving both processes of illness expression and adaptation, as well as pain having specific effects on the emotional state and behavioral function."[25(p101)]

IMPLICATIONS OF COMORBIDITY

Implications of comorbidity can be viewed from various perspectives: (1) the form of depressive presentations in primary care, (2) the recognition of depression in health care, and health services utilization, (3) impairments and disabilities, and (4) course and outcome.

Presentation of Depressive Disorders in Primary Care

Taking into account the significant association of depressive disorders with physical conditions, it is not surprising to see that the vast majority of depressed patients visiting primary care physicians do not openly present

Table 4. Utilization of Mental Health Services by Sector and Country[a]

% of Subjects With a 12-Month Major Depressive Episode	Sector					
	General Medical			Mental Health		
	United States	Canada	Germany	United States	Canada	Germany
Users in total sample[b]	9.8	25.8	30.5	20.8	28.9	28.8
Users with appropriate treatment[c]	19.5	21.0	16.3	26.0	32.9	28.8
Population with appropriate treatment	1.9	5.4	1.8	5.4	9.5	11.3

[a]Data from reference 27 and H.-U.W., unpublished data.
[b]Adjusted for age, gender, and education.
[c]Defined as antidepressants and 4 or more visits in past 12 months.

Table 5. Commonly Prescribed Psychiatric Treatment for ICD-10 Current Depression in Different Centers[a]

Center	% Recognized Among ICD-10 Current Depression Cases[b]	% Prescribed an Antidepressant	% Prescribed a Sedative	% Prescribed Any Other Drug	% Prescribed Any Nondrug Treatment
Ankara	28.2	19.4	29.0	32.0	45.2
Athens	32.4	9.1	45.5	27.2	45.5
Bangalore	46.2	21.7	21.7	13.3	15.0
Berlin	56.5	11.4	5.7	34.3	80.0
Groningen	63.2	15.2	16.5	15.2	74.7
Ibadan	63.0	0.0	35.3	23.5	94.1
Mainz	59.4	10.5	23.7	36.8	84.2
Manchester	64.3	38.6	12.9	18.8	85.1
Nagasaki	19.2	40.0	20.0	20.0	20.0
Paris	65.9	31.8	49.4	42.3	41.2
Rio de Janeiro	48.4	5.1	33.9	13.6	74.6
Santiago	72.6	18.8	40.0	22.3	61.2
Seattle	66.1	46.3	7.3	21.9	68.3
Shanghai	24.6	0.0	14.3	7.1	0.0
Verona	23.7	25.0	64.3	14.3	60.7
All centers	39.1	22.2	27.6	23.2	61.8

[a]Data from reference 26.
[b]Recognized by physician as psychological case.

with psychological problems. Thus, the recognition of depressive disorders may often be a considerable challenge to the treating physician.

In the WHO primary care study,[26] the majority of attendees complained primarily of some somatic symptoms (41%), 37% about pains, and 12% about fatigue and sleep problems. Additionally, the high comorbidity rates with somatoform and anxiety disorders, frequently dominated by somatic symptoms and complaints, may contribute considerably to the masking of depression, resulting in poor recognition and diagnosis of depressive disorders. From a health system perspective it is important to consider that there are noteworthy variations between sites and countries. For example, the northern European sites involved in this study (Paris, Groningen, Manchester, Verona, Mainz, and Berlin) all revealed higher than average findings concerning psychological, fatigue, and sleep problems compared with those of the United States and other sites.

Unfortunately, to date, no studies have systematically examined the effect of specific somatic illnesses comorbid with depression on the form of presentation and, more generally, illness behavior. However, preliminary data analyses of the abovementioned NMS[24] suggest that the effects of such comorbid patterns differ considerably by the type of somatic illness and its duration.

Recognition, Treatment, and Service Utilization

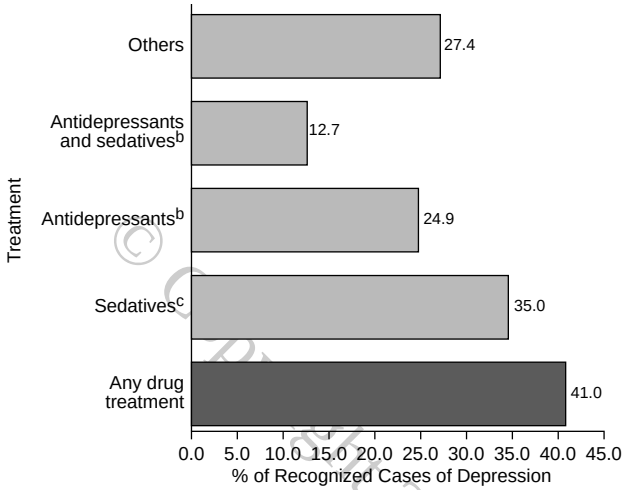
Depressive disorders have consistently been found to be poorly recognized and treated across all studies. In terms of population studies, Katz et al.[27] recently conducted a reanalysis of the health services utilization data relating to the diagnosis of major depression from the NCS[10] and Ontario Health Survey.[28] These 2 studies use similar assessment strategies as do the recent EDSP data from Germany.[12] A comparison of the findings is presented in Table 4.

Of patients with a current 12-month diagnosis of major depression, only 9.8% of the U.S. population contacted any general medical sector service, compared with 25.8% in Canada[27] and 30.5% in Germany (H.-U.W., unpublished data). Closer similarities were noted in the proportion of subjects with a major depressive episode who contacted specialized mental health services (20.8% for the United States to 28.9% for Canada). However, in all countries studied, no more than one third of patients in contact with either type of sector received what the authors define broadly as appropriate treatment (more than 4 visits as well as a prescription for antidepressants), resulting in extremely poor overall treatment rates of less than 10% of patients affected in all 3 countries. Katz et al.[27] also concluded that the overall lower probability of the U.S. population to receive appropriate treatment is possibly linked to health care insurance characteristics.

The WHO primary care study[26] (Table 5) impressively confirms these unfavorable data. Across centers, only 39.1% of primary care attendees with an ICD-10 diagnosis of a depressive episode were recognized as being a case with a "psychological disorder," and considerably fewer as specifically with a depressive disorder.

Of those recognized, approximately one fifth (22.2%) of patients across all centers received any antidepressants, with more patients receiving sedatives (27.6%) or other drug treatments (23.2%). The most frequently recorded single intervention was "unspecific counseling" (61.8%).[26] The authors conclude that there is little relation between

Figure 1. Which Type of Drug Treatment Was Prescribed? A Similar Picture (European Countries, DEPRES 1997)[a]



[a]Data from reference 29 and data on file, SmithKline Beecham.
Abbreviation: DEPRES = Depression Research in European Society study.
[b]64% of all antidepressants were tricyclic antidepressants.
[c]Sedatives are strongly related to anxiety complaints.

drug selection and any particular diagnosis. Antidepressants were prescribed with similar frequency for major depression as for any other diagnosis, and both the large proportion of sedative prescription rates for depression cases as well as the low antidepressant prescription rates were a concern. This interpretation basically holds true for all centers involved, despite the considerable variation between centers with regard to correct recognition rates and the proportions with drug prescriptions. Sartorius et al.[8] demonstrated in a further analysis of this dataset that comorbidity is a major factor in the frequent prescription of sedatives and other drugs, including multidrug treatment, in depressive disorders. Similar findings were recently reported in the Depression Research in European Society (DEPRES) study (Figure 1).[29] Almost identical low prescription rates of antidepressants (24.9%) and high rates for sedatives, both alone and in combination with antidepressants, were highlighted. Secondary analyses further confirmed that sedative prescription rates were strongly related to the presence of anxiety syndromes.

Burden of Comorbid Depression: Impairment and Disability

There is considerable evidence that comorbidity with depression has a remarkable effect on associated impairments and disabilities. Ormel et al.[23,30] demonstrated in the Groningen Longitudinal Aging Study (GLAS) study that comorbid depression significantly affects the degree of physical functioning, impairments in activities of daily living, social role functioning, numbers of inactivity hours, and life satisfaction (Table 6). The authors conclude that (1) comorbid depression in medical illness is strongly associated with poor functioning in both chronic and nonchronic medical conditions; (2) behavioral outcomes were strongly related to depression (and not primarily to the medical condition), particularly with persistent back (and other) pains, neurologic conditions (stroke, Parkinson's disease, multiple sclerosis), and joint conditions (arthritis); and (3) none of the medical conditions accounted for more variance in behavioral outcomes than did depression.

The dramatic effect of comorbidity on depression-specific impairments and disabilities has not only been demonstrated repeatedly in several general population surveys,[11,12] but also in primary care. Ormel et al.[31] used data based on the Brief Disability Schedule and the Social Disability Schedule from the WHO primary care study[9] to demonstrate that, of all "pure" depressive disorders in primary care, 39% revealed severe occupational disabilities and 46%, physical disabilities. The mean number of disability days was 6.1 during the past month for subjects with pure depressive disorders, but increased to 7.7 days for subjects with comorbid depression. The odds ratio of having occupational dysfunction/disability or physical dysfunction/disability increased with the number of comorbid mental disorders such that patients with 2 or more disorders saw an increase in disability measures 3.5 to 8.2 times that of a reference group. Similar increases in disabilities were demonstrated for depressive disorders comorbid with severe physical illnesses and were more pronounced for chronic diseases (Figure 2).

These findings clearly emphasize that the type and degree of comorbidity have considerable consequences not only for the social functioning of the individual, but also for society as a whole.

Course and Outcome

There is considerable evidence from various clinical and epidemiologic studies that comorbidity influences the course and outcome of depressive disorders. Wittchen et al.[6] found, in a comparison of clinical and epidemiologic data, that subjects with a lifetime comorbidity of anxiety and depression had lower psychosocial functioning scores (Global Assessment Scale), lower remission scores and considerably less frequently a favorable long-term course and outcome over 7 years compared with those with pure depressive disorders (Table 7). In a more elaborate analysis, this group also demonstrated that both the average length and the number of depressive episodes are significantly increased in comorbid depression.

Kessler et al.,[11] using data from the NCS, also confirmed that nonremission of depression is significantly more likely in subjects with a prior history of anxiety disorders. Furthermore, comorbid depression is more likely to result in hospitalization as well as in an increased risk of suicide attempts (Figure 3).

Table 6. Adjusted Mean Functioning and Well-Being by Medical Condition Status and Depressive Symptoms[a]

Outcome by Age Group	A No Medical Condition and No Depression	B No Medical Condition but Depression	p Value	C Medical Condition but No Depression	D Medical Condition and Depression	p Value
Age group, N						
57 y and older	1473	151		2887	768	
57–64 y	649	61		950	171	
65–74 y	573	52		1149	306	
75 y or older	248	38		784	289	
Mean score by age group						
MOS physical function[b]	81.7 (0.7)[d]	71.5 (2.0)[d]	.001	65.6 (0.5)[d]	48.6 (0.9)[d]	.001
57–64 y	89.5	80.5	.001	74.0	57.7	.001
65–74 y	84.6	68.5	.001	66.2	48.0	.001
75 y or older	71.5	65.1	.144	51.6	36.5	.001
GARS (I)ADL[c]	20.5 (0.2)	21.9 (0.6)	.001	23.1 (0.1)	27.7 (0.3)	.001
57–64 y	18.7	20.4	.001	20.7	23.9	.001
65–74 y	19.5	21.1	.010	22.2	27.2	.001
75 y or older	22.2	24.2	.067	27.4	32.2	.001
MOS role functioning[b]	91.4 (1.0)	78.6 (3.2)	.001	70.9 (0.7)	49.3 (1.4)	.001
57–64 y	94.7	86.5	.006	76.2	57.6	.001
65–74 y	95.1	77.6	.001	74.6	49.8	.001
75 y or older	86.6	71.4	.015	56.5	37.5	.001
SFL role functioning[c]	1.1 (0.1)	1.7 (0.2)	.001	2.3 (0.1)	4.0 (0.1)	.001
57–64 y	1.7	2.8	.002	2.9	4.8	.001
65–74 y	0.9	1.5	.021	1.9	3.6	.001
75 y or older	1.1	0.6	.167	2.0	3.6	.001
Subjective well-being[b]	34.2 (0.1)	31.2 (0.3)	.001	32.5 (0.1)	29.2 (0.1)	.001
57–64 y	34.4	32.1	.001	33.1	29.7	.001
65–74 y	34.5	30.7	.001	32.4	28.9	.001
75 y or older	33.6	31.7	.013	31.9	28.9	.001

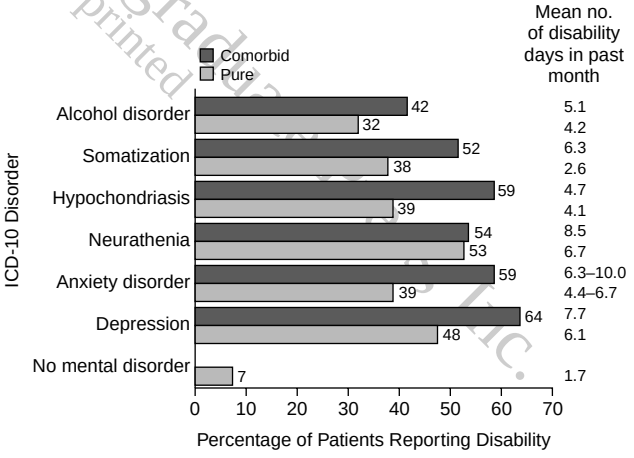
[a]Data from reference 23. Abbreviations: GARS (I)ADL = Groningen Activity Restriction Scale (Instrumental) Activation of Daily Living, MOS = Medical Outcomes Study, SFL = Social Functioning Limitation. Means are adjusted for gender, age, and socioeconomic status per pair of groups (A and B; C and D).
[b]Higher score indicates better functioning and well-being.
[c]Higher score indicates poorer functioning and well-being.
[d]Standard error within parentheses.

Although these findings concur with reports from clinical samples of comorbid cases with somatic illnesses (such as cancer[16,20] and cardiovascular diseases[21]) showing an increased mortality in comorbid depression, present findings in primary care are less consistent. Poorer course and outcome have been reported[32–34] with inconsistent or negative findings.[35–37] It seems that this variability in findings may be due to study design and other methodological considerations.

CONCLUSIONS

Major depression is an episodic and sometimes chronic disorder, associated in its active phases with a considerable degree of impairment and disability. Major depression is also frequently comorbid with a wide range of other mental and physical disorders. Such overlap has been impressively documented to have significant effects on the presentation of mental disorders in primary care, their recognition by doctors, symptom severity, and the resulting disability. The overall burden of comorbid depression in the general population, and particularly in primary care, has been shown to be substantially greater than that of pure disorders. This relates to both the patient in subjective suffering, resulting disabilities, and the course and outcome of illness and the health care system in use of services and financial burden.

Figure 2. Disability (moderate or severe occupational role dysfunction) by Current Pure and Comorbid Mental Disorder[a]



[a]Data from reference 31.

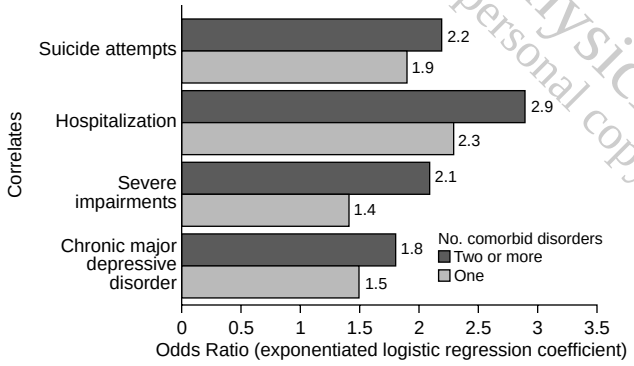
Considering comorbidity with mental disorders, it is particularly noteworthy that anxiety disorders and somatoform disorders are almost always temporally pri-

Table 7. Seven-Year Course and Outcome Characteristics in Pure and Comorbid Anxiety Disorders: A Comparison of Epidemiologic and Clinical Cases[a]

	Pure Anxiety		Pure Depression		Comorbid Anxiety and Depression	
Variable	Epidemiologic (N = 42)	Clinical (N = 19)	Epidemiologic (N = 40)	Clinical (N = 19)	Epidemiologic (N = 35)	Clinical (N = 59)
7-year outcome						
Global assessment of functioning (GAS), mean score	79.1	66.4	70.8	74.3	65.9	67.0
Remitted past 6 months, %	38.1	15.8	40.0	26.3	28.6	11.9
Pattern of course, %						
Favorable	54.2	50.0	74.1	36.8	29.4	28.8
Intermediate	30.8	11.1	18.7	36.8	52.5	27.1
Unfavorable	9.0	38.9	7.2	26.3	18.0	44.2
Missing	6.0	…	…	…	…	…

[a]Adapted from reference 6, with permission. Abbreviation: GAS = Global Assessment Scale.

Figure 3. The Effects of Primary Comorbidity on Persistence and Severity of Major Depressive Disorder[a]



[a]Data from reference 11.

mary disorders. Both conditions are highly prevalent in primary care settings across the world—however rarely recognized and poorly treated—and the frequency of their diagnostic overlap calls for routine assessments of depressive disorders in patients with signs of anxiety, as well as vice versa. This double routine screening might lead to improved overall recognition rates in primary care and might also give rise to more frequent adequate treatment strategies. However, the "mixed" nature of presenting complaints of comorbid depression in primary care will continue to be a challenge for primary care physicians, calling for further research and the development of more satisfactory diagnostic tools.

There is a still a considerable deficit in studies examining and evaluating the pattern of comorbidity between depressive disorders and somatic illnesses. Although studies in aged (65 years and older) populations suggest that for all subjective outcome measures examined, depression seems to outrank the relevance of somatic disorders in terms of unique and shared risk contribution, these findings need to be replicated with general population samples and for disease-specific pathways.

REFERENCES

1. Burke JD, Wittchen H-U, Regier DA, et al. Extracting information from diagnostic interviews on co-occurrence of symptoms of anxiety and depression. In: Maser JD, Cloninger CR, eds. Comorbidity of Mood and Anxiety Disorders. Washington, DC: American Psychiatric Press; 1990: 649–667
2. Wittchen H-U. Critical issues in the evaluation of comorbidity. Br J Psychiatry 1996;168(suppl 30):9–16
3. Wittchen H-U, Knäuper B, Kessler RC. Lifetime risk of depression. Br J Psychiatry 1994;165(suppl 26):16–22
4. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third Edition. Washington, DC: American Psychiatric Association; 1980
5. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
6. Wittchen H-U, Essau CA, Krieg JC. Anxiety disorders: similarities and differences of comorbidity in treated and untreated groups. Br J Psychiatry 1991;159(suppl 12):23–33
7. Merikangas KR, Angst J, Eaton W, et al. Comorbidity and boundaries of affective disorders with anxiety and substance misuse: results of an international task force. Br J Psychiatry 1996;168(suppl 30):58–67
8. Sartorius N, Üstün TB, Lecrubier Y, et al. Depression comorbid with anxiety: results from the WHO study on psychological disorders in primary health care. Br J Pychiatry 1996;168(suppl 30):38–43
9. Üstün TB, Sartorius N, eds. Mental Illness in General Health Care: An International Study. Chichester, England: Wiley; 1995
10. Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 1994;51:8–19
11. Kessler RC, Nelson CB, McGonagle KA, et al. Comorbidity of DSM-III-R major depressive disorder in the general population: results from the US National Comorbidity Survey. Br J Psychiatry 1996;168(suppl 30):17–30
12. Wittchen H-U, Nelson CB, Lachner G. Prevalence of mental disorders and psychosocial impairments in adolescents and young adults. Psychol Med 1998;28:109–126
13. Schuster P. Zunahme von Depressionen in jüngeren Geburtskohorten [dissertation]. Marburg, Germany: Philips-Universität. In press
14. Wittchen H-U, Kessler RC, Lieb R, et al. When Is Onset? Investigations in Early Developmental Stages of Anxiety and Depressive Disorders. American Psychiatric Press. In press
15. Musselman DL, Nemeroff CB. Depression and endocrine disorders: focus on the thyroid and adrenal system. Br J Psychiatry 1996;168(suppl 30): 123–128
16. Sonino N, Fava GA. Psychological aspects of endocrine disease [review]. Clin Endocrinol 1998;49:1–7
17. Maj M. Depressive syndromes and symptoms in subjects with human immunodeficiency virus (HIV) infection. Br J Psychiatry 1996;168(suppl 30):117–122
18. Atkinson JH, Grant I, Kennedy CJ, et al. Prevalence of psychiatric disorders among men infected with human immunodeficiency virus: a controlled study. Arch Gen Psychiatry 1988;45:859–864
19. McDaniel JS, Nemeroff CB. Depression in the cancer patient: diagnostic, biological, and treatment aspects. In: Chapman CR, Foley KM, eds. Current and Emerging Issues in Cancer Pain: Research and Practice. New York, NY: Raven Press; 1993:1–19
20. Spiegel D. Cancer and depression. Br J Psychiatry 1996;168(suppl 30): 109–116
21. Frasure-Smith N, Lesperance F, Talajic M. Depression following myocardial infarction: impact on 6-month survival. JAMA 1993;270:1819–1825
22. Wells JE, Bushnell JA, Hornblow AR, et al. Christchurch Psychiatric Epidemiology Study, part I: methodology and lifetime prevalence for specific psychiatric disorders. Aust N Z J Psychiatry 1989;23:315–326

23. Ormel J, Kempen GI, Deeg DJ, et al. Functioning, well-being and health perception in late middle-aged and older people: comparing the effects of depressive symptoms and chronic medical conditions. J Am Geriatr Soc 1998;46:39–48
24. Wittchen H-U, Müller N, Stroz S. Psychische Störungen: Häufigkeit, psychosoziale Beeinträchtigungen und Zusammenhänge mit körperlichen Erkrankungen. Deutsches Gesundheitswesen 1998;2:95–100
25. Von Korff M, Simon G. The relationship between pain and depression. Br J Psychiatry 1996;168(suppl 30):101–108
26. Üstün TB, Von Korff M. Primary mental health services: access and provision of care. In: Üstün TB, Sartorius N, eds. Mental Illness in General Health Care: An International Study. Chichester, England: Wiley; 1995: 347–360
27. Katz SJ, Kessler RC, Lin E, et al. Medication management of depression in the United States and Ontario. J Gen Intern Med 1998;13:77–85
28. Lin E, Goering P, Offord DR, et al. The use of mental health services in Ontario: epidemiologic findings. Can J Psychiatry 1996;41:572–577
29. Lepine J-P, Gastpar J, Mendlewicz J, et al. Depression in the Community: the first pan-European study, DEPRES (Depression Research in European Society). Int Clin Psychopharmacol 1997;12:19–29
30. Ormel J, Kempen GI, Penninx BW, et al. Chronic medical conditions and mental health in older people: disability and psychosocial resources mediate specific mental health effects. Psychol Med 1997;27:1065–1077
31. Ormel J, Von Korff M, Üstün TB, et al. Common mental disorders and disability across cultures: results from the WHO Collaborative Study on Psychological Problems in General Health Care. JAMA 1994;272:1741–1748
32. Sherbourne CD, Wells KB, Meredith LS, et al. Comorbid anxiety disorder and the functioning and well-being of chronically ill patients of general medical providers. Arch Gen Psychiatry 1996;53:889–895
33. Zung WWK, Magruder-Habib K, Velez R, et al. The comorbidity of anxiety and depression in general medical patients: a longitudinal study. J Clin Psychiatry 1990;51(6, suppl):77–80
34. Pini S, Tansella M, Wittchen H-U, et al. Prevalence, recognition and 12-month outcome of mental disorders in primary care. Am J Psychiatry. In press
35. Brown GW, Harris TO, Eales MJ. Social factors and comorbidity of depressive and anxiety disorders. Br J Psychiatry 1996;168(suppl 30):50–57
36. Simon GE, Von Korff M. Recognition, management, and outcome of depression in primary care. Arch Fam Med 1995;4:99–105
37. Tiemens BG, Ormel J, Simon GE. Occurrence, recognition and outcome of psychological disorders in primary care. Am J Psychiatry 1996;153: 636–644