Major Depressive Disorder and Axis I Diagnostic Comorbidity

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Background: Recognition of comorbid conditions in patients presenting for the treatment of depression is clinically important because the presence of other disorders can influence treatment planning. In the present study, we examined the frequency of diagnostic comorbidity in psychiatric outpatients presenting for treatment of nonbipolar major depressive disorder (MDD) and patients' desire for treatment for the comorbid disorders.

Method: Four hundred seventy-nine psychiatric outpatients with DSM-IV nonbipolar MDD were evaluated with a modified version of the Structured Clinical Interview for DSM-IV.

Results: Excluding nicotine dependence, at the time of the evaluation 64.1% (N = 307) of the patients met criteria for at least 1 of the 23 specific Axis I disorders, and more than one third (36.7%, N = 176) had 2 or more disorders. Anxiety disorders, as a group, were the most frequent current comorbid disorders (56.8%), and social phobia was the most frequent individual disorder. Including subthreshold conditions, the percentage of patients with at least 1 disorder increased to 73.5%. When the scope of assessment was expanded to include nicotine dependence, nicotine dependence was the most frequent lifetime individual disorder (38.2%) and the second most frequent current disorder (27.3%). There was considerable variability among the disorders regarding desire for treatment of the comorbid condition.

Conclusion: The majority of nonbipolar depressed patients have a current comorbid disorder, especially an anxiety disorder, although the actual rate of comorbidity depends on the breadth of the assessment.

(J Clin Psychiatry 2002;63:187–193)

Recognition of comorbid conditions in patients presenting for the treatment of depression is clinically important because the presence of other disorders can influence treatment planning. Because of the potential clinical significance of diagnostic comorbidity, it is important for clinicians to be aware of the frequency of specific comorbid conditions in depressed patients. While there are at least 20 studies of the frequency of the full range of specific DSM-III and DSM-III-R Axis II personality disorders in depressed patients,[1–20] we are aware of only 1 study of a wide range of Axis I disorders in nonbipolar depressed patients.[21]

In the present study from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project, we examined the frequency of diagnostic comorbidity in psychiatric outpatients presenting for treatment of nonbipolar major depressive disorder (MDD). Our focus is on *current* DSM-IV Axis I disorders because these more often have immediate clinical implications, although we also present lifetime rates so the findings can be compared with those from other studies of diagnostic comorbidity. Five questions were examined: (1) How often do depressed patients have at least 1 other current DSM-IV Axis I disorder at the time of presentation? (2) What is the impact of the breadth of assessment on the overall comorbidity rate? We examined the impact of 2 factors related to the breadth of assessment—the range of disorders covered and the assessment of subthreshold conditions. Because our diagnostic evaluation used an expanded version of the Structured Clinical Interview for DSM-IV (SCID),[22] we could compare the comorbidity rate based on the range of disorders typically covered by the

SCID with the rate based on a more complete evaluation of Axis I disorders. Subthreshold, or not otherwise specified (NOS), conditions have rarely been described in studies of diagnostic comorbidity. We found that many depressed patients presenting for treatment had clinically significant symptoms of a nondepressive disorder that never met full diagnostic criteria; therefore, we considered it important to describe this phenomenon in order to better appreciate the number of current comorbid conditions in depressed patients. Current subthreshold disorders also include conditions that met full criteria in the past but at the time of presentation had incompletely improved. Thus, we also examined the frequency of disorders that are in partial remission at the time of presentation. (3) How many depressed patients with a comorbid disorder have only 1 comorbid diagnosis, and how many patients have multiple comorbid conditions? (4) What is the frequency of each of the DSM-IV disorders, and how often does each disorder occur as the only comorbid condition? (5) How often do patients want treatment to address their comorbid condition? This last question highlights the importance, from the patient's perspective, of detecting diagnostic comorbidity in patients with a principal diagnosis of MDD.

METHOD

One thousand three hundred psychiatric outpatients were evaluated with a semistructured diagnostic interview in the Rhode Island Hospital Department of Psychiatry outpatient practice (Providence, R.I.). This private practice group predominantly treats individuals with medical insurance (including Medicare but not Medicaid) on a fee-for-service basis, and it is distinct from the hospital's outpatient residency training clinic that predominantly serves lower-income, uninsured, and medical assistance patients.

The patients were interviewed by a trained diagnostic rater who administered a modified version of the SCID. The Rhode Island Hospital institutional review committee approved the research protocol, and all patients provided informed, written consent. Only a minority of patients evaluated in the practice received the SCID because of the lack of available diagnostic raters or patients' preference for a less time-consuming standard clinical evaluation. As described elsewhere,[23] patients who did and did not participate in the study were similar in gender, education, marital status, and scores on self-administered symptom questionnaires.

Diagnostic raters included Ph.D.-level psychologists and research assistants with college degrees in the social or biological sciences. Research assistants received 3 to 4 months of training during which they observed at least 20 interviews, and they were observed and supervised in their administration of more than 20 evaluations. Psychologists observed only 5 interviews, and they were observed and supervised in their administration of 15 to 20

evaluations. During the course of training, the senior author (M.Z.) met with each rater to review the interpretation of every item on the SCID. Also during training, every interview was reviewed on an item-by-item basis by the senior rater, who observed the evaluation, and by the senior author, who reviewed the case with the interviewer. At the end of the training period, the raters were required to demonstrate exact, or near exact, agreement with a senior diagnostician on 5 consecutive evaluations. Throughout the MIDAS project, ongoing supervision of the raters consisted of weekly diagnostic case conferences involving all members of the team. In addition, every case was reviewed by the senior author.

During the course of the study, joint-interview diagnostic reliability information was collected on 26 patients. For current Axis I disorders diagnosed in at least 2 patients (by at least 1 rater), the kappa coefficients were as follows: MDD ($\kappa = 1.0$), dysthymic disorder ($\kappa = 1.0$), bipolar disorder ($\kappa = 1.0$), nicotine dependence ($\kappa = 1.0$), panic disorder ($\kappa = 1.0$), social phobia ($\kappa = .87$), obsessive-compulsive disorder (OCD; $\kappa = 1.0$), specific phobia ($\kappa = 1.0$), generalized anxiety disorder (GAD; $\kappa = .64$), and posttraumatic stress disorder (PTSD; $\kappa = 1.0$).

The core of the diagnostic evaluation was the January 1995 DSM-IV patient version of the SCID.[22] The Axis I version of the SCID covers 7 DSM-IV sections comprising mood, psychotic, substance use, anxiety, somatoform, adjustment, and eating disorders. We made several modifications to the SCID. First, after the first 100 patients were interviewed, modules were added for the impulse-control disorders (intermittent explosive disorder, kleptomania, pathological gambling, trichotillomania, and pyromania). Second, from the beginning of the study, we included a module assessing nicotine dependence. Third, the SCID screening question for social phobia was supplemented with questions about 12 specific social situations. Regardless of how individuals responded to the SCID screening probe about anxiety related to public speaking or eating in front of others, they were also asked if they felt more fearful, anxious, or nervous than most people when saying something in a group of people, business meetings, one-on-one conversations, etc. Sixteen depressed patients who answered "no" to the SCID screening question were diagnosed with social phobia (13 current, 3 past). Finally, irrespective of how the patient responded to the SCID screening question for PTSD, patients were asked about the presence of 11 specific traumatic events. Nine depressed patients who answered "no" to the SCID PTSD screening question were diagnosed with PTSD (3 current, 4 partial remission, 2 past).

NOS diagnoses were made in 2 ways. First, an NOS diagnosis was made in patients with clinically meaningful symptoms that fell below the DSM-IV symptom threshold to diagnose a specific disorder (e.g., PTSD criteria A, B, and C were met but only 1 criterion from the PTSD hyper-

arousal cluster was present). Although the DSM-IV symptom threshold was not met, the DSM-IV threshold for clinically significant distress or impairment was the same as that used for disorders meeting full inclusion criteria. When making these NOS diagnoses, we indicated to which specific disorder the NOS diagnosis was related (e.g., subthreshold panic disorder, subthreshold anorexia nervosa). The second way for patients to be given a current NOS diagnosis was when full DSM-IV criteria for a disorder were met in the past, but the symptoms had partially, but not completely, remitted. Although DSM-IV provides specific guidelines regarding use of a partial remission specifier only for the mood and substance use disorders, we adopted this specifier for all disorders. For example, someone who met DSM-IV criteria for PTSD 5 years ago but at the time of the evaluation was bothered by a subthreshold number of criteria would be diagnosed with the disorder in partial remission. As with the NOS diagnoses, the residual symptoms had to cause clinically meaningful impairment or distress to warrant a partial remission diagnosis. We examined the impact of both methods of making NOS diagnoses on the overall estimate of the frequency of comorbid disorders in depressed patients.

For the first 400 patients interviewed, the end of each SCID module included the following question about reason for seeking treatment: "Was (symptoms of disorder) a reason for coming for treatment now?" After the first 400 patients, we changed our methodology and asked 2 questions: "Was (symptoms of disorder) one of the main reasons you decided to seek treatment now? IF NO: Now that we've talked about (symptoms of disorder), would you like your treatment here to address these symptoms?" When asking these questions, the interviewer reviewed the features of the disorder that had just been described so the patient understood to what the question referred. In our analysis of desire for treatment, we combined the data for the entire sample.

RESULTS

Four hundred seventy-nine patients presented with a chief complaint of depression and were given a principal diagnosis of nonbipolar MDD. The group included 159 men (33.2%) and 320 women (66.8%) who ranged in age from 18 to 76 years (mean ± SD = 39.2 ± 12.0 years). Nearly half of the subjects were married (N = 205, 42.8%); the remainder were single (N = 128, 26.7%), divorced (N = 80, 16.7%), separated (N = 39, 8.1%), widowed (N = 8; 1.7%), or living with someone as if in a marital relationship (N = 19, 4.0%). About two thirds (65.8%, N = 315) had high school degrees or equivalency, 10.6% (N = 51) did not graduate from high school, and 23.6% (N = 113) graduated from a 4-year college. The sample was predominantly white (85.0%, N = 407). The mean ± SD Global Assessment of Functioning (GAF)[24]

score of the patients was 50.2 ± 9.2. More than two thirds of the patients had experienced at least 1 prior episode of MDD (N = 323, 67.4%), and the median duration of the current episode was 52 weeks.

The data in Table 1 show the frequency of current and lifetime Axis I disorders meeting full criteria in the 479 depressed outpatients. Excluding nicotine dependence, at the time of the evaluation 64.1% (N = 307) of the patients met criteria for at least 1 of the 23 specific Axis I disorders, and more than one third (36.7%, N = 176) had 2 or more disorders. Anxiety disorders, as a group, were the most frequent current comorbid disorder (56.8%), and social phobia was the most frequent individual disorder (32.4%). The majority of patients with at least 1 current disorder had more than 1 (57.3%, 176/307). The mean ± SD number of current comorbid Axis I disorders was 1.29 ± 1.34. Of the disorders diagnosed in at least 10 patients, the most frequent disorders to occur as the sole comorbid conditions were dysthymic disorder, panic disorder with agoraphobia, social phobia, and GAD, although only 25% of patients with these comorbid conditions had these as the sole comorbidity. On the other hand, OCD, specific phobia, alcohol abuse/dependence, body dysmorphic disorder, and intermittent explosive disorder rarely occurred as the sole comorbid condition.

The mean ± SD number of lifetime Axis I disorders was 2.12 ± 1.73, and most patients with at least 1 lifetime disorder had more than 1 (73.9%, 283/383). The current and lifetime prevalence rates of the disorders were generally comparable except for those for substance use disorders, which were the most common disorders that occurred in the past and had remitted by the time of the evaluation.

When the scope of assessment was expanded to include nicotine dependence, nicotine dependence was the most frequent lifetime individual disorder (38.2%) and the second most frequent current disorder (27.3%). When nicotine dependence is included in the comorbidity count, the percentage of patients with at least 1 current disorder increases from 64.1% to 72.2%, and the mean ± SD number of current Axis I disorders increases from 1.29 ± 1.34 to 1.56 ± 1.45. Including nicotine dependence in the determination of lifetime comorbidity, a mean of 2.50 ± 1.88 comorbid disorders were diagnosed, and 85.4% of the depressed patients had a lifetime history of a comorbid disorder.

Sixty-seven patients (14.0%) had an Axis I disorder that was in partial remission at the time of the evaluation. The data in Table 2 show that the most frequent disorders in partial remission were PTSD and alcohol dependence. When patients with an Axis I disorder in partial remission are included, the frequency of any comorbid disorder increases from 72.2% to 73.9%, and the mean ± SD number of disorders increases from 1.56 ± 1.45 to 1.72 ± 1.54. If nicotine dependence is excluded from this analysis, the

Table 1. Prevalence of Current and Lifetime DSM-IV Axis I Disorders in 479 Depressed Outpatients

Disorder	Total Current		Without Another Current Axis I Disorder[a]		Total Lifetime		Without Another Lifetime Axis I Disorder[a]	
	N	%	N	%	N	%	N	%
Mood disorders								
Dysthymic disorder	40	8.4	10	25.0	45	9.4	8	17.8
Anxiety disorders								
Panic disorder without agoraphobia	16	3.3	4	25.0	21	4.4	2	9.5
Panic disorder with agoraphobia	64	13.4	11	17.2	91	19.0	8	8.8
Agoraphobia without history of panic	4	0.8	1	25.0	6	1.3	3	50.0
Social phobia	155	32.4	39	25.2	173	36.1	21	12.1
Specific phobia	57	11.9	7	12.3	62	12.9	4	6.5
Posttraumatic stress disorder	62	12.9	13	21.0	103	21.5	7	6.8
Acute stress disorder	1	0.2	1	100.0	3	0.6	1	33.3
Generalized anxiety disorder	77	16.1	21	27.3	77	16.1	8	10.4
Obsessive-compulsive disorder	43	9.0	5	11.6	56	11.7	2	3.6
Any anxiety disorder	272	56.8	…	…	311	64.9	…	…
Substance use disorders								
Alcohol abuse/dependence	29	6.1	4	13.8	181	37.8	25	13.8
Drug abuse/dependence	22	4.6	4	18.2	107	22.3	5	4.7
Nicotine dependence	131	27.3	39	29.8	183	38.2	26	14.2
Any drug/alcohol use disorder	43	9.0	…	…	205	42.8	…	…
Any drug/alcohol/nicotine use disorder	159	33.2	…	…	289	60.3	…	…
Eating disorders								
Anorexia nervosa	0	0.0	0	0.0	3	0.6	0	0.0
Bulimia nervosa	4	0.8	3	75.0	17	3.5	1	5.9
Any eating disorder	4	0.8	…	…	19	4.0	…	…
Somatoform disorders								
Somatization disorder	3	0.6	0	0.0	3	0.6	0	0.0
Conversion disorder	1	0.2	0	0.0	1	0.2	0	0.0
Hypochondriasis	6	1.3	0	0.0	7	1.5	0	0.0
Pain disorder	5	1.0	3	60.0	5	1.0	1	20.0
Body dysmorphic disorder	10	2.1	0	0.0	11	2.3	0	0.0
Any somatoform disorder	23	4.8	…	…	25	5.2	…	…
Impulse-control disorders								
Intermittent explosive disorder	13	2.7	2	15.4	28	5.8	3	10.7
Trichotillomania	1	0.2	1	100.0	3	0.6	0	0.0
Pathological gambling	5	1.0	2	40.0	11	2.3	1	9.1
Kleptomania	0	0.0	0	0.0	2	0.4	0	0.0
Any impulse-control disorder	19	4.0	…	…	43	9.0	…	…

[a]Nicotine dependence was not considered when determining whether the disorder occurred as the sole comorbid condition. The denominator is the number of patients with the comorbid condition in question. For example, 25% of the 40 patients with dysthymic disorder did not have another comorbid Axis I disorder.

frequency of any comorbid condition that meets full criteria or is in partial remission is 66.8% and the mean number of Axis I disorders is 1.44 ± 1.44.

More than 20% (N = 107, 22.3%) of the patients had a current subthreshold NOS disorder. Consistent with the prevalence of disorders meeting full criteria or partial remission, subthreshold anxiety disorders were the most frequent NOS diagnoses (14.6%; Table 3). If NOS diagnoses are included as comorbid conditions, the percentage of patients with at least 1 disorder increases from 66.8% to 73.5% when nicotine dependence is not included and from 73.9% to 79.3% when nicotine dependence is included. The mean number of current comorbid Axis I disorders, including partial remissions, NOS diagnoses, and nicotine dependence was 1.97 ± 1.63. Table 4 summarizes the findings on the impact of the breadth of assessment on comorbidity rates.

There was considerable variability among the disorders regarding desire for treatment of the comorbid condition

(Table 5). Of the anxiety disorders, depressed patients usually wanted treatment of comorbid panic disorder, GAD, and PTSD. Two thirds of patients wanted treatment of social phobia and OCD, and about half wanted treatment of a specific phobia. Approximately half the patients with drug and alcohol problems wanted treatment to address these disorders, although desire for treatment of nicotine dependence was lower.

Patients with current disorders in partial remission frequently expressed a desire for treatment of these disorders. For example, 17 (53.1%) of the 32 patients with PTSD in partial remission desired treatment, as did 8 (57.1%) of the subjects with panic disorder in partial remission. Similarly, patients with problems that did not meet DSM-IV criteria for a full syndrome often desired treatment for these subthreshold conditions (e.g., 76.9% with subthreshold PTSD, 86.7% with subthreshold panic disorder, 63.3% with subthreshold eating disorder, 80% with undifferentiated somatoform disorder).

Table 2. Prevalence of DSM-IV Axis I Disorders in Partial Remission in 479 Depressed Outpatients

Disorder	N	%
Mood disorders		
Dysthymic disorder	0	0.0
Anxiety disorders		
Panic disorder without agoraphobia	4	0.8
Panic disorder with agoraphobia	10	2.1
Agoraphobia without history of panic	0	0.0
Social phobia	1	0.2
Specific phobia	1	0.2
Posttraumatic stress disorder	32	6.7
Acute stress disorder	0	0.0
Generalized anxiety disorder	0	0.0
Obsessive-compulsive disorder	1	0.2
Any anxiety disorder	47	9.8
Substance use disorders		
Alcohol abuse/dependence	11	2.3
Drug abuse/dependence	5	1.0
Nicotine dependence	1	0.2
Any drug/alcohol use disorder	14	2.9
Any drug/alcohol/nicotine use disorder	15	3.1
Eating disorders		
Anorexia nervosa	1	0.2
Bulimia nervosa	6	1.3
Any eating disorder	7	1.5
Somatoform disorders		
Somatization disorder	0	0.0
Conversion disorder	0	0.0
Hypochondriasis	0	0.0
Pain disorder	0	0.0
Body dysmorphic disorder	1	0.2
Any somatoform disorder	1	0.2
Impulse-control disorders		
Intermittent explosive disorder	1	0.2
Trichotillomania	0	0.0
Pathological gambling	0	0.0
Kleptomania	0	0.0
Any impulse-control disorder	1	0.2

Table 3. Prevalence of DSM-IV Axis I Not Otherwise Specified (NOS) Disorders in 479 Depressed Outpatients

Disorder	N	%
Anxiety disorders		
Subthreshold panic disorder	15	3.1
Subthreshold social phobia	3	0.6
Subthreshold specific phobia	2	0.4
Subthreshold posttraumatic stress disorder	39	8.1
Subthreshold generalized anxiety disorder	9	1.9
Subthreshold obsessive-compulsive disorder	2	0.4
Mixed anxiety depression disorder	0	0.0
Other NOS anxiety disorder	4	0.8
Any NOS anxiety disorder	70	14.6
Eating disorders		
Subthreshold anorexia nervosa	4	0.8
Subthreshold bulimia nervosa	6	1.3
Binge eating disorder	14	2.9
Other NOS eating disorder	6	1.3
Any NOS eating disorder	30	6.3
Somatoform disorders		
Undifferentiated somatoform disorder	15	3.1

When we recomputed the comorbidity rate limiting the assessment to the disorders assessed by Sanderson et al., the rates were almost identical (60.1% of the present sample had a current disorder). Methodological issues notwithstanding, it is reasonable to conclude that the majority of nonbipolar depressed patients have a current comorbid Axis I disorder and that, as a class, anxiety disorders are the most frequent current disorders.

We are not aware of any previous study of comorbidity rates of current disorders that has discussed how to classify individuals who have partially remitted from a disorder. This is not an issue in studies of lifetime diagnostic comorbidity. Across all disorders, 14% of the patients had a current disorder that was in partial remission. The most frequent condition in partial remission was PTSD. The significance of these symptoms to the patient is reflected by the relatively high desire for treatment of these residual PTSD symptoms (53.1%). Similarly, 57.1% of the 14 patients with panic disorder in partial remission wanted treatment to address this disorder.

Comorbidity studies also rarely include NOS categories. We will look at the validity of NOS categories in another publication; however, it is worth noting the relatively high frequency of some NOS diagnoses (subthreshold PTSD, panic disorder, eating disorder, and undifferentiated somatoform disorder). In fact, NOS diagnoses were more frequent than partial remission diagnoses. As with disorders in partial remission, there was a relatively high frequency with which patients wanted treatment for problems that did not meet the DSM-IV criteria for the full syndrome (subthreshold PTSD, 76.9%; subthreshold panic disorder, 86.7%; subthreshold eating disorder, 63.3%; undifferentiated somatoform disorder, 80.0%). This is not surprising considering that these diagnoses were made only when the diagnostic interviewer determined that a clinically significant level of impairment or distress was present.

DISCUSSION

From a clinical perspective, it is important to know the frequency of disorder co-occurrence when such co-occurrence might influence treatment selection or predict the chronicity of the primary disorder. However, it is not straightforward to estimate the rate of diagnostic comorbidity. There is no single answer to the question posed in the introduction, "How often do depressed patients have at least 1 other current DSM-IV Axis I disorder?"

Diagnostic comorbidity rates will vary between studies because they are influenced by several methodological factors such as the number of disorders assessed, method of assessment (semistructured interview vs. clinical evaluation), time period covered (current vs. lifetime), handling of partial remissions, and inclusion of NOS categories. Even when standardized assessments are used, rates will vary between studies because of differences in the breadth of the evaluation.

In the present study, we found that 79.3% of patients had a current comorbid disorder. This was 20% higher than the rate reported by Sanderson and colleagues.[21]

Table 4. Summary of Current and Lifetime DSM-IV Axis I Comorbidity Rates in 479 Depressed Outpatients As a Function of the Breadth of the Diagnostic Assessment[a]

	Total		1 or More Disorders		2 or More Disorders	
Diagnosis	Mean	SD	N	%	N	%
Current						
Dysthymic, anxiety, substance, somatoform, eating disorders	1.25	1.30	302	63.0	170	35.5
All of above + impulse-control disorders	1.29	1.34	307	64.1	176	36.7
All of above + nicotine dependence	1.56	1.45	346	72.2	207	43.2
All of above + partial remission	1.72	1.54	354	73.9	229	47.8
All of above + NOS disorders	1.97	1.63	380	79.3	257	53.6
Lifetime						
Dysthymic, anxiety, substance, somatoform, eating disorders	2.03	1.68	378	78.9	272	56.8
All of above + impulse-control disorders	2.12	1.73	383	80.0	283	59.1
All of above + nicotine dependence	2.50	1.88	409	85.4	312	65.1
All of above + NOS disorders	2.81	1.94	426	88.9	343	71.6

[a]Abbreviation: NOS = not otherwise specified.

Table 5. Desire for Treatment for Current DSM-IV Axis I Comorbid Disorders in 479 Depressed Outpatients

Disorder	Frequency of the Disorder, N	Desire for Treatment	
		N	%
Mood disorders			
Dysthymic disorder	40	38	95.0
Anxiety disorders			
Panic disorder without agoraphobia	16	14	87.5
Panic disorder with agoraphobia	64	53	82.8
Agoraphobia without history of panic	4	2	50.0
Social phobia	155	106	68.4
Specific phobia	57	29	50.8
Posttraumatic stress disorder	62	51	83.6
Acute stress disorder	1	1	100.0
Generalized anxiety disorder	77	70	90.9
Obsessive-compulsive disorder	43	28	65.1
Substance use disorders			
Alcohol abuse/dependence	29	17	58.6
Drug abuse/dependence	22	12	54.5
Nicotine dependence	131	51	38.9
Eating disorders			
Anorexia nervosa	0	0	00.0
Bulimia nervosa	4	3	75.0
Somatoform disorders			
Somatization disorder	3	1	33.3
Conversion disorder	1	1	100.0
Hypochondriasis	6	3	50.0
Pain disorder	5	4	80.0
Body dysmorphic disorder	10	7	70.0
Impulse-control disorders			
Intermittent explosive disorder	13	9	69.2
Trichotillomania	1	1	100.0
Pathological gambling	5	5	100.0
Kleptomania	0	0	0.0

The treatment and prognostic implications of comorbidity in depressed patients have been inadequately researched. Some studies find that comorbidity is associated with poorer outcome,[25–31] whereas other studies fail to demonstrate the negative prognostic significance of comorbidity.[32,33] Many of these studies use a naturalistic, longitudinal follow-up design; few are placebo-controlled treatment studies. Most placebo-controlled studies of the efficacy of antidepressant medications exclude patients with comorbid conditions from participation, although the number and type of Axis I disorders that are the basis for exclusion vary among studies.[34–39] In light of the high frequency of diagnostic comorbidity, this raises questions about the generalizability of the literature on the efficacy of antidepressant medications. It is unknown whether those patients who are excluded from efficacy trials due to diagnostic comorbidity (who make up the majority of depressed patients treated in routine clinical practice) would demonstrate an active drug-placebo differential response rate. This supports the recent calls for effectiveness research that uses less restrictive inclusion and exclusion criteria to select subjects.[40]

Knowledge of a comorbid Axis I disorder in depressed patients influences the choice of an antidepressant medication.[41] It seems appropriate to preferentially choose a selective serotonin reuptake inhibitor (SSRI) over tricyclic antidepressants (TCAs) when treating a depressed patient with OCD or social phobia because SSRIs but not TCAs have been found to be effective in treating these disorders.[42,43] However, whether SSRIs would prove superior to TCAs when depression is complicated by these comorbid conditions has received little research attention. The best empirically supported impact on treatment choice is the preferential selection of an SSRI over a TCA in the treatment of depressed patients with comorbid OCD.[44]

Antidepressant dosing also might be influenced by the presence of comorbid conditions. For example, lower initial dosages of SSRIs may be appropriate when treating depressed patients with comorbid panic disorder,[45] although no controlled data support this recommendation.

The present sample was drawn from a large, general, adult outpatient private practice setting in which patients had medical insurance. Relatively few minority patients are seen in the practice. It will be important to replicate and extend the present findings to samples with different demographic and clinical characteristics.

In conclusion, the results of this study indicate that most psychiatric outpatients presenting for the treatment of nonbipolar MDD have 1 or more current Axis I disorders, the most frequent of which are the anxiety disorders. The exact frequency of diagnostic comorbidity in depression depends, in part, on the number of disorders evaluated and whether subthreshold disorders are included. The importance of comorbidity from the patients' perspective is suggested by their desire to have treatment address their

comorbid conditions. The treatment implications of comorbidity in depressed patients warrant future study.

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