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ORIGINAL ARTICLE

Diagnostic co-morbidity in 2300 psychiatric out-patients presenting for treatment evaluated with a semi-structured diagnostic interview

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Background. The largest clinical epidemiological surveys of psychiatric disorders have been based on unstructured clinical evaluations. However, several recent studies have questioned the accuracy and thoroughness of clinical diagnostic interviews; consequently, clinical epidemiological studies, like community-based studies, should be based on standardized evaluations. The Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project is the largest clinical epidemiological study using semi-structured interviews assessing a wide range of psychiatric disorders conducted in a general clinical out-patient practice. In the present report we examined the frequency of DSM-IV Axis I diagnostic co-morbidity in psychiatric out-patients.

Method. A total of 2300 out-patients were interviewed with the Structured Clinical Interview for DSM-IV (SCID) upon presentation for treatment.

Results. The mean number of current and lifetime DSM-IV Axis I disorders in the 2300 patients was 1.9 (S.D. = 1.5) and 3.0 (S.D. = 1.8) respectively. The majority of patients were diagnosed with two or more current disorders, and more than one-third were diagnosed with three or more current disorders. Examination of the most frequent current disorders in the patients with the 12 most common principal diagnoses indicated that the pattern of co-morbidity differed among the disorders. The highest mean number of current co-morbid disorders was found for patients with a principal diagnosis of post-traumatic stress disorder and bipolar disorder.

Conclusions. Clinicians should assume that psychiatric patients presenting for treatment have more than one current diagnosis. The pattern of co-morbidity varies according to the principal diagnosis.

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Key words: Clinical epidemiology, co-morbidity, diagnosis.

Introduction

Contemporary studies of diagnostic co-morbidity generally fall into three types. First are the community-based epidemiological studies such as the Epidemiologic Catchment Area study (Robins *et al*. 1991), the National Co-morbidity Study (Kessler *et al*. 1994) and the National Epidemiologic Survey on Alcohol and Related Conditions (Grant *et al*. 2004), which are based on sophisticated sampling methodologies to ascertain a representative sample of the general population, and use lay interviewers to administer fully structured instruments to determine the presence of about 20 psychiatric disorders. These community-based studies of psychiatric disorders provide important information about the public health burden of these problems, the frequency of their co-occurrence, and the correlates of co-morbidity. However, although the frequency of treatment seeking for psychiatric disorders may be increasing (Olfson *et al*. 2002), most patients in the community do not get treatment for psychiatric disorders (Narrow *et al*. 1993; Kessler *et al*. 1999). Because seeking treatment is related to a number of clinical, social and demographic factors (Alegria *et al*. 2000; Goodwin *et al*. 2002), studies of the frequency and correlates of psychiatric disorders in the general population should be replicated in clinical populations to provide the practicing clinician with information that might have more direct clinical utility.

The second type of study of co-morbidity is based on unstructured clinical evaluations of psychiatric patients. Some large, single-site, clinical epidemiological studies have been conducted based on clinical diagnoses (Koenigsberg *et al*. 1985; Mezzich *et al*. 1989; Oldham & Skodol, 1991). However, several recent studies have questioned the accuracy and

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thoroughness of unstructured clinical diagnostic interviews because, compared to research interviews, co-morbidity rates based on unstructured interviews are much lower (Zimmerman & Mattia, 1999*a*; Basco *et al*. 2000; Shear *et al*. 2000; Miller *et al*. 2001).

The third type of co-morbidity study is the clinical epidemiological study using research-quality diagnostic instruments. There are many studies of co-morbidity of this type in patients with one or a limited number of index diagnoses, often conducted in research settings or clinics specializing in the treatment of particular disorders (Sierles *et al*. 1983; Barlow *et al*. 1986; DeRuiter *et al*. 1989; Green *et al*. 1989; Cassano *et al*. 1990; Sanderson *et al*. 1990*a*, *b*; Turner *et al*. 1991; Brown & Barlow, 1992; Schwalberg *et al*. 1992; Goisman *et al*. 1995; Fava *et al*. 2000; Wilfley *et al*. 2000; Brown *et al*. 2001; McElroy *et al*. 2001; Melartin *et al*. 2002; Perugi *et al*. 2002; Diniz *et al*. 2004). There are few studies of co-morbidity in an unselected large series of patients presenting for treatment in an out-patient practice that do not focus on the treatment of specific disorders. The dearth of such studies may be related, in part, to the obstacles that must be overcome in integrating comprehensive research assessments into a general clinical practice. Nonetheless, because the presence of co-morbid conditions has clinically significant implications, such as predicting prognosis (Keller *et al*. 1984; Coryell & Noyes, 1988; Coryell *et al*. 1988; Grunhaus, 1988; Noyes *et al*. 1990) and influencing psychiatrists' selection of medication (Zimmerman *et al*. 2004, 2005), it is important to derive estimates of co-morbidity rates in individuals presenting for psychiatric treatment.

To the best of our knowledge the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project is the largest clinical epidemiological study using semi-structured interviews to assess a wide range of psychiatric disorders conducted in a general clinical out-patient practice (Zimmerman & Mattia, 1999*a*, 2000). Among the strengths of the study are that diagnoses are based on the reliable and valid procedures used in research studies, and the patients are presenting to a community-based psychiatric out-patient practice rather than a research clinic specializing in the treatment of one or a few disorders. The aims of the present report from the MIDAS project were fourfold. First, we described the frequency distribution of the number of current DSM-IV Axis I disorders in a large sample of psychiatric out-patients presenting for treatment. Second, we determined the current prevalence of specific DSM-IV Axis I disorders, how often the disorders were diagnosed as the principal diagnosis, and how often they were diagnosed as an additional, co-morbid condition. Third, when a disorder was the principal diagnosis, we examined how often it was the sole diagnosis and how often co-morbid conditions were diagnosed. Fourth, we examined co-morbidity with specific disorders for the most frequent principal diagnoses.

Table 1. *Demographic characteristics of 2300 psychiatric out-patients*

Gender, *n* (%)	
Female	1392 (60.5)
Male	908 (39.5)
Education, *n* (%)	
Less than high school	232 (10.1)
Graduated high school	1467 (63.8)
Graduated college or greater	601 (26.1)
Marital status, *n* (%)	
Married	941 (40.9)
Living with someone	122 (5.3)
Widowed	42 (1.8)
Separated	132 (5.7)
Divorced	347 (15.1)
Never married	716 (31.1)
Race, *n* (%)	
White	2015 (87.6)
Black	100 (4.3)
Hispanic	57 (2.5)
Asian	18 (0.8)
Portuguese	77 (3.3)
Other	33 (1.4)
Age (years), mean (S.D)	38.2 (12.8)

Method

The MIDAS project represents an integration of research methodology into a community-based out-patient practice affiliated with an academic medical center (Zimmerman, 2003). A comprehensive diagnostic evaluation is conducted upon presentation for treatment. To date, 2300 patients have been recruited in the MIDAS project from the Rhode Island Hospital Department of Psychiatry out-patient practice. 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 out-patient residency training clinic, which predominantly serves lower income, uninsured and medical assistance patients. Data on referral source were recorded for the last 500 patients enrolled in the study. Patients were most frequently referred from primary care physicians (34.6%), psychotherapists (14.6%) and family members or friends (13.6%).

The data in Table 1 show the demographic characteristics of the sample. The majority of the subjects

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were white, female, married or single, and high school graduates. The mean age of the sample was 38.2 years (S.D. = 12.8).

Not all patients who presented for treatment participated in the study. Patients were offered the opportunity to have a more comprehensive evaluation as part of the clinical research program, although they were not required to undergo this evaluation. The varying number of trained diagnostic interviewers available influenced the number of patients who were invited to participate. Because one of the aims of the MIDAS project is to develop and study the reliability and validity of self-administered questionnaires, patients with significant cognitive limitations were not included; thus, we disproportionately excluded elderly patients. Nonetheless, as reported elsewhere, patients who did and did not participate in the study were similar in scores on self-administered symptom questionnaires (Zimmerman & Mattia, 1999*a*). Of particular importance, patients who did and did not participate in the MIDAS project did not differ in their scores on the Psychiatric Diagnostic Screening Questionnaire (PDSQ), a self-administered scale that screens for 13 DSM-IV Axis I disorders (Zimmerman & Mattia, 2001*a*, *b*).

Patients were interviewed by a diagnostic rater who administered a modified version of the Structured Clinical Interview for DSM-IV (SCID; First *et al*. 1995) and the Structured Interview for DSM-IV Personality (SIDP-IV; Pfohl *et al*. 1997). The diagnostic raters were highly trained and monitored throughout the project to minimize rater drift. Diagnostic raters included Ph.D.-level psychologists and research assistants with college degrees in the social or biological sciences. Research assistants received 3–4 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 only observed five interviews; however, they, too, were observed and supervised in their administration of 15–20 evaluations. During the course of training, the senior author met with each rater to review the interpretation of every item on the SCID and SIDP-IV. Also during training, every interview was reviewed on an item-by-item basis by the senior rater who observed the evaluation. At the end of the training period, the raters are required to demonstrate exact, or near exact, agreement with a senior diagnostician on five consecutive evaluations. Throughout the MIDAS project, ongoing supervision of the raters consisted of weekly diagnostic case conferences involving all members of the team. Written reports of all cases were reviewed by M.Z., who also reviewed the item ratings of every case. The Rhode Island Hospital institutional review committee approved the research protocol, and all patients provided informed, written consent.

The core of the diagnostic evaluation was the January 1995 DSM-IV patient version of the SCID (First *et al*. 1995). The Axis I version of the SCID covers seven DSM-IV sections: mood disorders [major depressive disorder (MDD), bipolar disorder, dysthymia, depressive disorder not otherwise specified (NOS), mood disorder due to a general medical condition, substance induced mood disorder], psychotic disorders (schizophrenia, schizophreniform disorder, delusional disorder, schizo-affective disorder, brief psychotic disorder, psychotic disorder NOS), substance use disorders (abuse and dependence of alcohol, sedative-hypnotics, cannabis, stimulants, opioids, cocaine, hallucinogens, inhalants, phenylcyclidine, polydrug), anxiety disorders [panic disorder with and without agoraphobia, agoraphobia without history of panic disorder, social phobia, specific phobia, obsessive–compulsive disorder (OCD), posttraumatic stress disorder (PTSD), acute stress disorder, generalized anxiety disorder (GAD), anxiety disorder NOS], somatoform disorders [somatization disorder, pain disorder, undifferentiated somatoform disorder, hypochondriasis, body dysmorphic disorder (BDD)], adjustment disorders, and eating disorders (anorexia nervosa, bulimia nervosa, binge eating disorder). The SCID does not cover childhood, cognitive, factitious, dissociative, sexual and gender identity, sleep, and impulse control disorders, or other conditions that may be the focus of clinical attention. However, information from the overview at the beginning of the interview could be used to diagnose these other disorders.

As an ongoing part of the MIDAS project, joint-interview diagnostic reliability information was collected on 48 participants. For disorders diagnosed in at least two patients by at least one of the two raters, the κ coefficients were: MDD ($\kappa = 0.91$, $n = 17$), dysthymic disorder ($\kappa = 0.88$, $n = 5$), bipolar disorder ($\kappa = 0.85$, $n = 4$), panic disorder ($\kappa = 1.0$, $n = 8$), social phobia ($\kappa = 0.84$, $n = 14$), OCD ($\kappa = 1.0$, $n = 4$), specific phobia ($\kappa = 0.91$, $n = 7$), GAD ($\kappa = 0.93$, $n = 9$), PTSD ($\kappa = 0.91$, $n = 7$), alcohol abuse/dependence ($\kappa = 0.64$, $n = 6$), drug abuse/dependence ($\kappa = 0.73$, $n = 5$), and any somatoform disorder ($\kappa = 1.0$, $n = 5$).

We followed the DSM-IV convention to distinguish between principal and additional diagnoses (Zimmerman & Mattia, 2000). That is, the principal diagnosis referred to the disorder that the patient indicated was the main reason for seeking treatment; all other diagnoses were considered additional diagnoses.

The prevalence of some disorders may have been influenced by some modifications of the SCID. First,

after the first 91 patients were interviewed, modules were added for the impulse control disorders [intermittent explosive disorder (IED), kleptomania, pathological gambling, trichotillomania and pyromania]. Second, the SCID screening question for social phobia was supplemented with questions about 12 specific social situations. Regardless of how individuals responded to the SCID's screening probe about anxiety regarding 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. Third, the SCID screening question for PTSD was followed by questions about 13 specific traumatic events that were asked regardless of how individuals responded to the screen. However, as reported elsewhere, few patients who responded negatively to the SCID screening question were diagnosed with PTSD (Franklin *et al*. 2002).

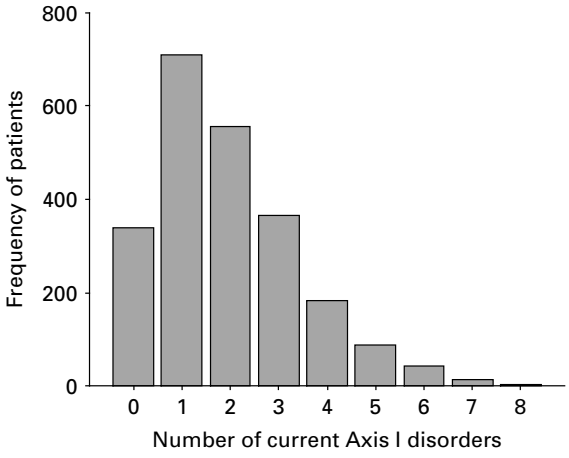

Fig. 1. Frequency of number of current DSM-IV Axis I disorders in 2300 psychiatric out-patients.

Data analysis

The degree of co-morbidity in a study will be influenced, in part, by the breadth of the assessment. *A priori* we chose not to include nicotine dependence when computing the mean number of disorders. The prevalence rates for current disorders did not include disorders that were in partial remission, or disorders that did not meet full criteria for a specific disorder (i.e. NOS disorders). We examined the frequency of co-morbid disorders in the 11 Axis I disorders diagnosed as the principal diagnosis in at least 1% of the sample. We used the χ^2 statistic to compare the rate of co-morbid disorders present in patients with and without each of these 11 disorders. We limited our analysis to disorders diagnosed as a co-morbid disorder in at least 1% of the sample.

Results

The mean number of current and lifetime DSM-IV Axis I disorders in the 2300 patients was 1.9 (S.D. = 1.5) and 3.0 (S.D. = 1.8) respectively. Figure 1 shows the distribution of the number of current diagnoses. Three hundred and fifty-five patients had no current Axis I diagnosis that met full diagnostic criteria. Of these 355 patients, 159 had an NOS disorder, 119 had an Axis I disorder in partial remission, 19 had a past Axis I disorder, 18 had a personality disorder, and 40 had no disorder. Of the 1945 patients with a current Axis I disorder, 36.7% (n = 714) had only one disorder, whereas 34.5% (n = 671) had three or more current Axis I diagnoses.

The data in Table 2 indicate that the most frequent Axis I disorder was MDD (45.0%). MDD was also the most common principal diagnosis, with more than three-quarters of the depressed patients having this as their principal diagnosis. The second most common diagnosis was social phobia. However, in contrast to MDD, which, when present, was usually the principal diagnosis, few patients with social phobia had it as their principal diagnosis. The other diagnoses that were present in at least 10% of the sample were PTSD, panic disorder, GAD and specific phobia. Only MDD, bipolar disorder and adjustment disorder were more frequently diagnosed as a principal disorder than as an additional disorder.

For the 11 disorders diagnosed as the principal disorder in more than 1% of the patients, we determined how often each was diagnosed as the sole disorder (Table 3). In these analyses disorders in partial remission and NOS diagnoses were not included. For all principal diagnoses except adjustment disorder, the majority of the patients had at least one co-morbid disorder. The highest mean number of co-morbid disorders was found for patients with a principal diagnosis of PTSD and bipolar disorder.

The data in Table 4 show the most frequent current disorders in the patients with the 11 most common principal diagnoses. It is noteworthy that the pattern of co-morbidity differs among the disorders. For example, patients with a principal diagnosis of MDD were significantly more likely than the non-depressed patients to also be diagnosed with dysthymic disorder and social phobia. Patients with a principal diagnosis of bipolar disorder experienced significantly higher rates of anxiety disorders, particularly social phobia, PTSD, GAD and OCD. Patients with a principal diagnosis of social phobia had the highest frequency of BDD, and patients with PTSD had the highest rate of

Table 2. *Frequency of current DSM-IV principal and additional diagnoses in 2300 psychiatric out-patients*

	Total		Principal diagnosis[a]		Additional diagnosis	
	n	%	*n*	%	*n*	%
Mood disorders						
Any mood disorder	1238	53.8				
Major depression	1034	45.0	810	78.3	224	21.7
Dysthymic disorder	174	7.6	45	25.9	129	74.1
Bipolar I disorder	44	1.9	42	95.4	2	4.6
Bipolar II disorder	78	3.4	66	84.6	12	15.4
Anxiety disorders						
Any anxiety disorder	1279	55.6				
Panic disorder	100	4.3	26	26.0	74	74.0
Panic disorder with agoraphobia	313	13.6	99	31.6	214	68.4
Agoraphobia without history of panic	27	1.2	1	3.7	26	96.3
Social phobia	640	27.8	26	4.1	614	95.9
Specific phobia	239	10.4	4	1.7	235	98.3
Post-traumatic stress disorder	295	12.8	88	29.8	207	70.2
Generalized anxiety disorder	407	17.7	72	17.7	335	82.3
Obsessive–compulsive disorder	170	7.4	32	18.8	138	81.2
Substance use disorders						
Any substance use disorder	273	11.9				
Alcohol abuse/dependence	206	9.0	23	11.2	183	88.8
Drug abuse/dependence	110	4.8	10	9.1	100	90.9
Eating disorders						
Any eating disorder	75	3.3				
Anorexia nervosa	0	0	0	0	0	0
Bulimia nervosa	18	0.8	1	5.6	17	94.4
Binge eating disorder	57	2.5	2	3.5	55	96.5
Psychotic disorder						
Any psychotic disorder	30	1.3				
Schizophrenia	13	0.6	12	92.3	1	7.7
Schizo-affective disorder	13	0.6	12	92.3	1	7.7
Delusional disorder	4	0.2	2	50.0	2	50.0
Somatoform disorders						
Any somatoform disorder	163	7.1				
Somatization disorder	13	0.6	2	15.4	11	84.6
Hypochondriasis	27	1.2	9	33.3	18	66.7
Undifferentiated somatoform disorder	59	2.6	17	28.8	42	71.2
Pain disorder	21	0.9	7	33.3	14	66.7
Body dysmorphic disorder	55	2.4	7	12.7	48	87.3
Impulse control disorders[b]						
Any impulse control disorder	103	4.5				
Intermittent explosive disorder	75	3.3	15	20.0	60	80.0
Trichotillomania	9	0.4	0	0	9	100.0
Pathological gambling	17	0.7	7	41.2	10	58.8
Kleptomania	3	0.1	1	33.3	2	66.7
Adjustment disorders	129	5.6	114	88.4	15	11.6

[a] The principal diagnosis referred to the disorder that the patient indicated was the main reason for seeking treatment; all other diagnoses were considered additional diagnoses. The sum of all principal diagnoses is not 2300 because 40 patients received no current diagnoses, 442 patients received a current Axis I or Axis II principal diagnosis not included on the table, 229 patients received an Axis I principal diagnosis in partial remission, 25 patients received an Axis I principal diagnosis that was in remission, and 12 patients received a current Axis I or Axis II diagnosis but not a principal diagnosis because their reason for presenting for treatment was unrelated to a psychiatric diagnosis.

[b] Impulse control disorders were assessed in a subset of 2209 individuals of the total sample of 2300 individuals.

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Table 3. *Likelihood and degree of current Axis I co-morbidity in 2300 psychiatric out-patients with different principal diagnoses*[a]

			One disorder only		Co-morbid diagnoses	
Principal diagnosis	*n*	%	*n*	%	Mean	S.D.
Mood disorders						
Major depression	810	35.2	252	31.1	1.4	1.4
Dysthymic disorder	45	2.0	21	46.7	0.8	0.9
Bipolar I disorder	42	1.8	10	23.8	2.1	1.8
Bipolar II disorder	66	2.9	16	24.2	1.7	1.3
Anxiety disorders						
Panic disorder	26	1.1	11	42.3	0.9	1.3
Panic disorder with agoraphobia	99	4.3	19	19.2	1.6	1.4
Social phobia	26	1.1	6	23.1	1.5	1.2
Post-traumatic stress disorder	88	3.8	12	13.6	2.0	1.4
Generalized anxiety disorder	72	3.1	21	29.2	1.2	1.0
Obsessive–compulsive disorder	32	1.4	10	31.2	1.2	1.2
Adjustment disorders	114	5.0	78	68.4	0.4	0.7

S.D., Standard deviation.

[a] This table is limited to the 11 disorders diagnosed as the principal disorder in more than 1% of the patients.

co-morbid MDD and panic disorder with agoraphobia. Significantly lower rates of co-morbid mood and anxiety disorders were diagnosed in patients with adjustment disorder. Co-morbid substance use, eating, and somatoform disorders were not significantly higher in patients with any particular principal Axis I disorder.

Discussion

Co-morbidity is frequent in psychiatric out-patients. Other studies of single disorders, as well as general population community studies, have reported similar results. In most studies, however, lifetime rates of pathology are examined. Instead, we focused on current disorders because these are the ones that usually require the treating clinician's initial attention.

Exactly how frequent co-morbidity is in clinical practice depends, in part, on the breadth of assessment. We used the SCID to diagnose Axis I disorders, albeit a modified version of the SCID. The SCID only assesses a subset of the disorders included in the DSM-IV. We included impulse control disorders and BDD in our interview although the SCID does not cover these disorders. However, because these disorders had a relatively low prevalence, this modification of the SCID did not have a marked impact on estimates of overall co-morbidity. The SCID does not assess sleep and sexual disorders, and we did not write modules to assess these categories. Had these disorders been included, co-morbidity estimates would have been higher. We did not include disorders in partial remission, NOS specified diagnoses, and nicotine dependence in our estimates of co-morbidity. In a previous report from the MIDAS project on diagnostic co-morbidity in patients with MDD, we found that estimates of co-morbidity were significantly raised when these disorders were included (Zimmerman *et al*. 2002). Slightly more than one-third (35.5%) of the depressed patients had two or more additional diagnoses when co-morbidity estimates were based on the presence of current eating, anxiety, substance use, somatoform, or dysthymic disorder. After including disorders in partial remission, NOS diagnoses and nicotine dependence, more than half (53.6%) of the patients were diagnosed with two or more co-morbid disorders.

Despite limiting our analyses to current disorders that met full criteria for a specific DSM-IV disorder, the majority of patients were diagnosed with two or more disorders, and more than one-third were diagnosed with three or more disorders. Clinicians should assume that, in patients presenting for the treatment of mood or anxiety problems, the patient has more than one diagnosis. Co-morbidity burden was greatest in patients with principal diagnoses of PTSD and bipolar disorder.

In contrast to patients who met criteria for a specific mood or anxiety disorder, patients diagnosed with an adjustment disorder as principal usually did not have another disorder. Adjustment disorder is a residual category that is only diagnosed when the symptoms of anxiety and/or depression, occurring in the context of a stressful event, do not meet criteria for a specific

Table 4. *Frequency of current DSM-IV Axis I disorders in 2300 psychiatric out-patients with the most common Axis I disorders diagnosed as the principal diagnosis*

	Principal diagnosis										
Co-morbid disorder	MDD ($n=810$)	Dysthymic disorder ($n=45$)	Bipolar I disorder ($n=42$)	Bipolar II disorder ($n=66$)	Panic disorder ($n=26$)	Panic with agoraphobia ($n=99$)	Social phobia ($n=26$)	PTSD ($n=88$)	GAD ($n=72$)	OCD ($n=32$)	Adjustment disorder ($n=114$)
MDD	–	0 (0)	–	–	38.5 (10)	42.4 (42)	30.8 (8)	55.7 (49)[a]	22.2 (16)[d]	18.8 (6)[d]	0.9 (1)[d]
Dysthymic disorder	9.9 (80)[b]	–	0 (0)	0 (0)	0 (0)	3.0 (3)	15.4 (4)	6.8 (6)	4.2 (3)	3.1 (1)	0 (0)
Bipolar I	–	0 (0)	–	–	0 (0)	0 (0)	0 (0)	1.1 (1)	0 (0)	3.1 (1)	0 (0)
Bipolar II	–	0 (0)	–	–	0 (0)	2.0 (2)	3.8 (1)	4.5 (4)	0 (0)	0 (0)	0 (0)
Panic disorder	4.7 (38)	2.2 (1)	7.1 (3)	6.1 (4)	–	–	3.8 (1)	4.5 (4)	5.6 (4)	6.3 (2)	0 (0)
Panic disorder with agoraphobia	14.0 (113)	2.2 (1)[c]	19.0 (8)	21.2 (14)	–	–	0 (0)	22.7 (20)[a]	5.6 (4)[c]	3.1 (1)	0.9 (1)[d]
Agoraphobia without panic disorder	1.5 (12)	0 (0)	0 (0)	1.5 (1)	–	–	0 (0)	1.1 (1)	1.4 (1)	3.1 (1)	0 (0)
Social phobia	33.2 (269)[b]	22.2 (10)	50.0 (21)[b]	36.4 (24)	7.7 (2)[c]	32.3 (32)	–	35.2 (31)	34.7 (25)	28.1 (9)	8.8 (10)[d]
Specific phobia	11.9 (96)	6.7 (3)	19.0 (8)	12.1 (8)	15.4 (4)	13.1 (13)	15.4 (4)	18.2 (16)[a]	8.3 (6)	18.8 (6)	4.4 (5)[c]
PTSD	14.1 (114)	2.2 (1)[c]	31.0 (13)[b]	19.7 (13)	7.7 (2)	10.1 (10)	11.5 (3)	–	1.4 (1)[d]	6.3 (2)	1.8 (2) [d]
GAD	19.1 (155)	11.1 (5)	31.0 (13)[a]	27.3 (18)[a]	7.7 (2)	27.3 (27)[a]	19.2 (5)	12.5 (11)	–	9.4 (3)	4.4 (5)[d]
OCD	7.3 (59)	4.4 (2)	16.7 (7)[a]	15.2 (10)[a]	3.8 (1)	10.1 (10)	0 (0)	8.0 (7)	12.5 (9)	–	0.9 (1)[d]
Alcohol disorder	8.0 (65)	4.4 (2)	4.8 (2)	9.1 (6)	3.8 (1)	4.0 (4)	15.4 (4)	6.8 (6)	4.2 (3)	3.1 (1)	9.6 (11)
Drug use disorder	4.4 (36)	2.2 (1)	4.8 (2)	3.0 (2)	3.8 (1)	3.0 (3)	3.8 (1)	4.5 (4)	1.4 (1)	3.1 (1)	3.5 (4)
Binge eating disorder	3.1 (25)	2.2 (1)	4.8 (2)	6.1 (4)	0 (0)	2.0 (2)	3.8 (1)	1.1 (1)	2.8 (2)	0 (0)	1.8 (2)
Hypochondriasis	0.9 (7)	2.2 (1)	0 (0)	0 (0)	0 (0)	3.0 (3)	3.8 (1)	1.1 (1)	1.4 (1)	0 (0)	0 (0)
Undifferentiated somatoform disorder	2.7 (22)	4.4 (2)	2.4 (1)	1.5 (1)	0 (0)	2.0 (2)	0 (0)	0 (0)	2.8 (2)	3.1 (1)	0.9 (1)
BDD	2.5 (20)	4.4 (2)	4.8 (2)	1.5 (1)	0 (0)	3.0 (3)	15.4 (4)[b]	1.1 (1)	1.4 (1)	0 (0)	0 (0)
IED	3.0 (24)	0 (0)	4.8 (2)	1.5 (1)	3.8 (1)	3.0 (3)	0 (0)	5.7 (5)	4.2 (3)	0 (0)	1.8 (2)
Adjustment disorders	0 (0)	0 (0)	0 (0)	1.5 (1)	0 (0)	0 (0)	0 (0)	1.1 (1)	2.8 (2)	0 (0)	–

MDD, Major depressive disorder; PTSD, post-traumatic stress disorder; GAD, generalized anxiety disorder; OCD, obsessive–compulsive disorder; BDD, body dysmorphic disorder; IED, intermittent explosive disorder.

Values are given as % (n).

[a] Patients with principal diagnosis > all other patients, $p<0.05$.

[b] Patients with principal diagnosis > all other patients, $p<0.01$.

[c] Patients with principal diagnosis < all other patients, $p<0.05$.

[d] Patients with principal diagnosis < all other patients, $p<0.01$.

disorder. Thus, adjustment disorder falls lower on a diagnostic hierarchy than specific disorders because the diagnosis is excluded if criteria for another disorder such as MDD are met.

Some disorders, although frequent, were rarely the primary reason for seeking treatment. For example, social phobia was the second most frequent diagnosis, but less than 5% of the patients with social phobia received the diagnosis as the principal disorder. This has potential implications for studies of treatment efficacy. For disorders such as social phobia that are infrequently diagnosed as the principal disorder in clinical practice, it will be important for the next generation of treatment efficacy studies to determine if treatment is effective when the disorder is a co-morbid condition.

How do our data compare to the results of recent large-scale community-based epidemiological studies using DSM-IV criteria? In the European Study of the Epidemiology of Mental Disorders (ESEMeD) project, 12-month and lifetime prevalence rates were presented for 10 disorders (MDD, dysthymic disorder, panic disorder, agoraphobia, GAD, social phobia, specific phobia, alcohol abuse, and alcohol dependence) (The ESEMeD MHEDEA 2000 investigators, 2004; Alonso & Lepine, 2007). In general, the 12-month co-morbidity rates were lower in the ESEMeD study compared to the present study. Approximately half of the subjects with MDD in the ESEMeD sample had a co-morbid disorder, lower than the two-thirds rate in the MIDAS project. Slightly more than half of the ESEMeD subjects diagnosed with PTSD had a co-morbid disorder, whereas we found that almost 90% of the patients with a principal diagnosis of PTSD had at least one other current Axis I disorder. Nearly half of the subjects with social phobia in the ESEMeD project had a co-morbid disorder, whereas the corresponding rate in the MIDAS project was 77%. The only disorder with a higher co-morbidity rate in the ESEMeD project was dysthymia (73% *v.* 53%). Overall rates of co-morbidity and the percentage of subjects with three or more disorders were not reported for the ESEMeD project. By contrast, the NCS-R (Kessler *et al*. 2005) reported overall co-morbidity rates for the past 12 months among 20 disorders, but did not describe the likelihood of each disorder occurring in isolation. Approximately half of the patients with one disorder had at least one other disorder, lower than the 63% rate in the current study, and 27% had three or more disorders, lower than the 35% rate in the current study. The Australian National Survey of Mental Health and Well-Being is the only epidemiological study that examined current co-morbidity (Andrews *et al*. 2001), and it is also the only community study that distinguished principal from additional diagnoses (Andrews *et al*. 2002). The 12 disorders evaluated in this study included nine of the 10 disorders included in the ESEMeD project (specific phobia was not included), as well as drug abuse/dependence, and three personality disorder clusters (cluster A, cluster B, cluster C). Forty per cent of the subjects with a current disorder met criteria for another disorder, lower than the 63% rate in the current study of psychiatric out-patients. Subjects with a principal diagnosis of a mood disorder (MDD or dysthymia) were the most likely to have a co-morbid disorder (52.3%). Forty per cent of the patients with a principal diagnosis of an anxiety disorder had a co-morbid condition. Again, these figures are lower than the rates in the MIDAS project.

It is not surprising that our co-morbidity rates are higher than the rates reported in these three large community-based epidemiological studies. It has been known for a long time that co-morbidity is associated with seeking treatment (Berkson, 1946). Consistent with this, these studies found that co-morbidity was associated with increased rates of health service utilization as well as poorer psychosocial functioning (Andrews *et al*. 2001; Kessler *et al*. 2005; Alonso & Lepine, 2007). This highlights the importance of conducting clinical epidemiology studies because the co-morbidity rates in community studies do not apply to the rates found in clinical settings and are thus less informative to practicing clinicians.

Is it important for the clinician to detect diagnostic co-morbidity? The recognition of co-morbidity is not simply of academic interest, it has important clinical significance. For example, the co-occurrence of anxiety disorders in depressed patients has been associated with a more chronic course of depression in psychiatric patients, primary care patients, and epidemiological samples (Van Valkenberg *et al*. 1984; Coryell *et al*. 1988; Grunhaus, 1988; Brown *et al*. 1996; Fava *et al*. 1997; Sherbourne & Wells, 1997; Gaynes *et al*. 1999; Trivedi *et al*. 2006). Co-morbidity is also significant from another perspective – the patients' perspective. In an earlier report from the MIDAS project based on the first 400 patients enrolled in the study (and who are included in the present report), we reported that patients want treatment to address the symptoms of their co-morbid disorders (Zimmerman & Mattia, 2000). Thus, from a consumer perspective, detecting co-morbid disorders is important.

The type of diagnostic interview conducted will affect estimates of co-morbidity rates. More diagnoses are made according to semi-structured interviews than unstructured clinical evaluations. Clinical studies of co-morbidity have reported relatively low co-morbidity rates (Stangler & Printz, 1979; Mezzich *et al*. 1987; Loranger, 1990; Basco *et al*. 2000). Despite very

different patient groups, the results of studies using unstructured interviews were essentially identical – not more than one in four patients received at least one additional diagnosis. This is less than half the rate based on research interviews. Using structured interviews, evidence indicates that 50–75% of patients receiving a diagnosis of PTSD, GAD, OCD, social phobia, MDD, dysthymia, specific phobia, or panic disorder with or without agoraphobia meet criteria for at least one additional diagnosis (Sierles *et al*. 1983; Barlow *et al*. 1986; DeRuiter *et al*. 1989; Green *et al*. 1989; Cassano *et al*. 1990; Sanderson *et al*. 1990*a*, *b*; Turner *et al*. 1991; Brown & Barlow, 1992; Schwalberg *et al*. 1992; Goisman *et al*. 1995; Fava *et al*. 2000; Wilfley *et al*. 2000; McElroy *et al*. 2001; Melartin *et al*. 2002; Perugi *et al*. 2002; Diniz *et al*. 2004).

Lower co-morbidity rates found in studies using unstructured clinical evaluations *versus* studies using structured research evaluations suggest that there may be a problem with under-recognition of co-morbidity in routine clinical settings. Some reports have directly demonstrated this to be the case with single diagnoses (Markowitz *et al*. 1991; Davidson & Smith, 1993). The MIDAS project was the first to broadly examine the problem of underdiagnosis across a range of disorders. Early reports from the MIDAS project documented problems with the thoroughness of standard clinical evaluations (Zimmerman & Mattia, 1999*a*–*c*). That is, fewer diagnoses were made by clinicians using an unstructured clinical interview compared to the administration of a semi-structured diagnostic interview such as the SCID. This research was subsequently independently replicated in other settings (Basco *et al*. 2000; Shear *et al*. 2000; Miller *et al*. 2001).

Another factor that can influence co-morbidity rates is the demographic and clinical profile of the patients evaluated. Questions of generalizability can be raised about the present study, as with every other clinical epidemiology study. In contrast to community-based epidemiological studies that use sophisticated sampling methods to ensure representation of the general population, clinical epidemiological studies are generally single-site studies of samples of convenience. The most frequent current Axis I diagnoses in the sample were mood and anxiety disorders, and relatively few patients had eating, somatoform, impulse control, substance use and psychotic disorders. However, the rank order of Axis I disorder frequency was generally similar to the findings in community-based epidemiological studies (Zimmerman & Mattia, 2000).

Although the recognition of diagnostic co-morbidity is clinically important, and several studies have demonstrated that clinicians under-recognize co-morbidity, from the outset of the MIDAS project we assumed that comprehensive semi-structured interviews were unlikely to be incorporated into other clinical practices. Thus, we developed a self-administered questionnaire, the PDSQ, to screen for the most common DSM-IV Axis I disorders diagnosed in out-patient settings (Zimmerman & Mattia, 1999*d*, 2001*a*, *b*; Zimmerman & Sheeran, 2003; Zimmerman & Chelminski, 2006). The aim was to develop a measure with good psychometric properties that was brief enough to be incorporated into routine clinical practice, and thereby enable clinicians to improve their detection of co-morbid disorders and also be more efficient in conducting their diagnostic evaluations. Recently, reports on the utility of the PDSQ in clinical practice have come from the STAR*D trial on the effectiveness of treating depression in psychiatric and primary care settings (Rush *et al*. 2005; Trivedi *et al*. 2006).

Before concluding, it is important to recognize that a limitation of the study was that it was conducted in a single clinical practice in which the majority of the patients were white, female, and had health insurance. Replication of the results in other clinical samples with different demographic characteristics is warranted. The strengths of the study are the large sample size, and the use of highly trained diagnostic interviewers to reliably administer a semi-structured diagnostic interview.

In conclusion, the results of this large clinical epidemiology study indicate that the majority of psychiatric patients have more than one current DSM-IV Axis I disorder. Another report from the MIDAS project suggested that patients usually want their treatment to address their co-morbid disorders. While there has been a great deal of discussion about co-morbidity in the two decades since the publication of DSM-III, relatively little treatment research has focused on patients with multiple disorders. We hope that by documenting the high frequency of co-morbidity in clinical practice, this will provide the impetus for modifying the exclusion criteria of treatment studies to allow patients with multiple disorders to be included, and to determine the outcome of co-morbid disorders as well as the index disorder that is being treated.

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Declaration of Interest

None.

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