

Generalized Anxiety Disorder

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Introduction

Generalized, chronic, ‘free-floating’ anxiety has been recognized as an important clinical condition for more than a century (Rickels & Rynn 2001). However, while there is strong agreement about the existence of generalized anxiety that is severe enough to warrant diagnosis and treatment, there is far less agreement about the features that define the condition and distinguish it from normal anxiety. This may be because anxiety is experienced occasionally by almost everyone, especially during times of stress. Furthermore, normal expressions of anxiety vary widely, with many people experiencing higher-than-average levels of anxiety without being considered to have a mental disorder.

Due in part to these challenges, the definition of generalized anxiety disorder (GAD) has changed more in the last three decades than perhaps any other mental disorder (Davidson *et al.* 2010). In its original instantiation in DSM-III (APA 1980), GAD was defined as persistent anxiety lasting at least one month and involving associated symptoms from three of four categories. As persistent anxiety is a feature of all anxiety disorders, GAD was treated as a ‘wastebasket’ or residual diagnostic category. It was assumed to be associated with relatively modest impairment. In DSM-III-R (APA 1987), GAD changed from a residual diagnosis to an independent disorder defined centrally by pathological worry. To facilitate discrimination from normal worry, the worry in GAD was defined as generalized (related to multiple life circumstances), excessive, unrealistic, and accompanied by six of 18 associated symptoms of anxiety. Minimum duration was increased from one to six months to distinguish GAD from transient stress reactions. DSM-IV (APA 1994) established generalized, excessive, uncontrollable worry as the cardinal feature of GAD. To sharpen the separation from other anxiety disorders, associated symptoms were restricted to six symptoms of tension and vigilance that were most frequently observed in GAD patients, with three required for diagnosis. The disturbance was required

to last at least six months and to cause clinically significant distress or impairment.

The DSM-IV conceptualization of GAD was widely viewed as an improvement over earlier definitions (Ballenger *et al.* 2001). The emphasis on worry and a streamlined set of associated symptoms aided clinicians in detecting GAD and distinguishing it from closely related disorders (Marten *et al.* 1993; Chelminski & Zimmerman 2003), helping to raise diagnostic reliability up to the level of other anxiety disorders (Brown *et al.* 2001). Despite these improvements, debates have persisted about the validity of GAD (Brown *et al.* 1994; Starcevic *et al.* 2012). A particularly controversial aspect of GAD has been its relationship with mood disorders, especially major depressive disorder (MDD). Although associations are strong between all anxiety and mood disorders, GAD and MDD overlap the most in their comorbidity (Ruscio & Khazanov, 2017), clinical features (Ehring & Watkins 2008; Watson 2009), and genetic risk (Kendler *et al.* 1992), leading some to question the distinctness of these disorders (see Goldberg *et al.*, 2010). DSM-IV dealt with the close relationship between GAD and mood disorders by including a diagnostic hierarchy rule that prohibited a diagnosis of GAD when its symptoms occurred exclusively during episodes of a mood disorder. The rationale was that depressed and manic individuals frequently present with heightened anxiety and agitation and that, when these symptoms wax and wane with other mood symptoms, they should be considered part of the mood disorder rather than an independent disorder (APA 1994). Although the hierarchy rule was intended to avoid extraneous diagnoses of GAD, subsequent clinical research suggested that cases subject to the hierarchy rule resembled patients with comorbid GAD-MDD much more closely than patients with MDD alone (Zimmerman & Chelminski 2003). Largely for this reason (Andrews *et al.* 2010), the hierarchical exclusion with mood disorders was dropped from the definition of GAD in the recently published DSM-5 (APA 2013).

This latest diagnostic revision has reopened questions about the validity of the GAD diagnosis and its separation from other mental disorders. It has also raised new questions about how GAD cases identified by DSM-IV differ from those identified by DSM-5. Comparing individuals diagnosed under the two systems is important not only for establishing the validity of the new GAD criteria, but for determining the likely generalizability of prior research findings and treatment guidelines to DSM-5 GAD, ensuring continuity of research and clinical care (see Abel & Borkovec 1995). To our knowledge, only two studies have compared GAD diagnosed with and without the hierarchy rule, both using outpatient samples in specialty mental health clinics in the United States (Zimmerman & Chelminski 2003; Lawrence *et al.* 2009). Those studies suggested that lifting the hierarchy rule yields a sizable number of new GAD cases and that the new cases are particularly severe, with a high burden of comorbidity and disability.

Although suggestive, these findings are limited in two important respects. First, help-seeking samples are known to differ systematically from the population at large in their severity and comorbidity (Berkson 1946). Representative community samples are not subject to these biases. In addition, because they include individuals who are not in treatment as well as those receiving treatment, community samples are well-suited to describing the proportion of those with a disorder who seek clinical care and the settings in which care is sought. Knowledge of these patterns aids clinicians in assessing and detecting GAD in a variety of service settings and aids policy-makers in estimating unmet need in the community. Second, data from countries other than the United States are needed. Most of what is known about GAD comes from a small number of economically developed countries (cf. Somers *et al.* 2006). Studying GAD in other parts of the globe is necessary, however, for separating universal features of the disorder from those that vary by country or culture (Lewis-Fernández *et al.* 2010). As the DSM system is intended to guide clinical diagnosis, treatment planning, and research and policy efforts around the world, cross-national information about the GAD diagnosis is critical.

In this chapter, we used data from the WMH surveys to describe DSM-IV GAD and compare it to DSM-5 GAD. By lifting the DSM-IV hierarchy rule barring the diagnosis of GAD during a mood disorder, we were able to compare cases identified by the two diagnostic systems within the same sample. We considered the

implications of the diagnostic revision for the prevalence of GAD, its comorbidity with other mental disorders, its associations with role impairment and treatment seeking, and its clinical course and socio-demographic correlates. We examined the generalizability of results by performing analyses not only in the large cross-national sample, but within subgroups of countries that differ in economic development.

Methods

Data from all 29 WMH surveys are included in this report. The combined sample included 147,261 respondents from 26 countries. As GAD was assessed in Part I, all analyses used the Part I sample except the comorbidity analyses, which were performed using the Part II sample to allow disorders assessed in Part II to be included.

The Composite International Diagnostic Interview (CIDI) 3.0 generates diagnoses of mental disorders using DSM-IV criteria. In the United States survey, lifetime GAD diagnoses based on the CIDI were shown to have good concordance with clinician-assigned diagnoses based on the Structured Clinical Interview for DSM-IV (SCID; First *et al.* 2002), with an area under the Receiver Operating Characteristic (ROC) curve (AUC) of 0.83 (Ruscio *et al.* 2005). Similar analyses in a subset of four WMH surveys did not evaluate GAD in isolation, but found good concordance between CIDI and SCID diagnoses of any 12-month anxiety disorder including GAD (AUC = 0.88; Haro *et al.* 2006).

CIDI diagnoses of DSM-IV GAD are assigned when excessive, uncontrollable worry is reported about a number of events or activities, accompanied by at least three of six associated symptoms, present more days than not for at least six months, and associated with significant distress or impairment; an additional requirement is that DSM-IV diagnostic hierarchy and organic exclusion rules must be met. DSM-5 GAD diagnoses generated for this chapter were identical to the DSM-IV diagnoses except that they allowed GAD to be diagnosed even when the symptoms occurred exclusively during episodes of a mood disorder.

Results

Prevalence

Prevalence increased substantially from DSM-IV to DSM-5 (Table 6.1). DSM-IV GAD has a lifetime

Table 6.1 Prevalence of DSM-IV and DSM-5 generalized anxiety disorder in the World Mental Health Surveys

Country	Lifetime prevalence					12-month prevalence					30-day prevalence					Sample size used
	DSM-IV		DSM-5		% change	DSM-IV		DSM-5		% change	DSM-IV		DSM-5		% change	
	%	SE	%	SE		%	SE	%	SE		%	SE	%	SE		
Low/lower-middle-income	1.1	(0.1)	1.6	(0.1)	45.5	0.6	(0.1)	0.9	(0.1)	50.0	0.3	(0.0)	0.5	(0.1)	66.7	36,498
Colombia	1.3	(0.3)	1.9	(0.3)	46.2	0.6	(0.2)	1.0	(0.2)	66.7	0.3	(0.1)	0.4	(0.1)	33.3	4,426
Iraq	3.7	(0.5)	5.0	(0.6)	35.1	2.3	(0.3)	3.0	(0.4)	30.4	1.4	(0.3)	2.0	(0.3)	42.9	4,332
Nigeria	0.1	(0.0)	0.1	(0.0)	0.0	0.03	(0.0)	0.03	(0.0)	0.0	–	–	–	–	0.0 ^a	6,752
Peru	0.7	(0.1)	1.1	(0.1)	57.1	0.2	(0.1)	0.5	(0.1)	150.0	–	–	0.1	(0.0)	– ^b	3,930
PRC (Beijing/Shanghai)	0.8	(0.1)	1.0	(0.1)	25.0	0.5	(0.1)	0.6	(0.1)	20.0	0.3	(0.1)	0.3	(0.1)	0.0	5,201
PRC (Shenzhen)	0.1	(0.0)	0.2	(0.1)	100.0	0.04	(0.0)	0.1	(0.1)	150.0	–	–	–	–	0.0 ^a	7,132
Ukraine	2.0	(0.2)	3.3	(0.3)	65.0	1.0	(0.1)	2.1	(0.2)	110.0	0.6	(0.1)	1.3	(0.1)	116.7	4,725
Upper-middle-income	2.1	(0.1)	2.8	(0.1)	33.3	1.1	(0.1)	1.6	(0.1)	45.5	0.4	(0.0)	0.7	(0.1)	75.0	28,927
Brazil	3.7	(0.3)	5.1	(0.4)	37.8	2.3	(0.2)	3.3	(0.3)	43.5	1.0	(0.1)	1.8	(0.2)	80.0	5,037
Bulgaria	1.7	(0.2)	2.3	(0.2)	35.3	0.9	(0.1)	1.2	(0.1)	33.3	0.3	(0.1)	0.5	(0.1)	66.7	5,318
Colombia (Medellín)	2.6	(0.4)	3.8	(0.5)	46.2	1.2	(0.3)	2.1	(0.3)	75.0	0.4	(0.1)	0.9	(0.2)	125.0	3,261
Lebanon	2.0	(0.3)	2.3	(0.3)	15.0	1.2	(0.3)	1.5	(0.3)	25.0	0.5	(0.2)	0.6	(0.2)	20.0	2,857
Mexico	0.9	(0.1)	1.1	(0.2)	22.2	0.4	(0.1)	0.6	(0.1)	50.0	0.2	(0.1)	0.3	(0.1)	50.0	5,782
Romania	0.8	(0.2)	1.0	(0.3)	25.0	0.2	(0.1)	0.2	(0.1)	0.0	0.1	(0.1)	0.2	(0.1)	100.0	2,357
South Africa	2.5	(0.3)	3.6	(0.4)	44.0	1.4	(0.2)	1.9	(0.3)	35.7	0.4	(0.1)	0.6	(0.1)	50.0	4,315
High-income	3.7	(0.1)	5.0	(0.1)	35.1	1.5	(0.1)	2.3	(0.1)	53.3	0.6	(0.0)	0.9	(0.0)	50.0	81,836
Australia	6.0	(0.4)	8.0	(0.5)	33.3	2.2	(0.3)	3.6	(0.3)	63.6	0.8	(0.2)	1.5	(0.2)	87.5	8,460
Belgium	1.9	(0.4)	2.8	(0.5)	47.4	0.6	(0.2)	0.9	(0.3)	50.0	0.2	(0.1)	0.3	(0.1)	50.0	2,419
France	4.9	(0.5)	6.2	(0.5)	26.5	1.5	(0.3)	2.1	(0.3)	40.0	0.5	(0.2)	0.6	(0.2)	20.0	2,894
Germany	1.1	(0.2)	1.5	(0.2)	36.4	0.3	(0.1)	0.5	(0.1)	66.7	0.2	(0.1)	0.2	(0.1)	0.0	3,555
Israel	3.3	(0.3)	4.4	(0.3)	33.3	2.2	(0.2)	3.1	(0.3)	40.9	0.7	(0.1)	1.1	(0.2)	57.1	4,859
Italy	1.4	(0.2)	2.1	(0.3)	50.0	0.4	(0.1)	0.6	(0.1)	50.0	0.1	(0.0)	0.2	(0.1)	100.0	4,712
Japan	1.9	(0.2)	2.6	(0.3)	36.8	0.9	(0.1)	1.2	(0.2)	33.3	0.1	(0.1)	0.2	(0.1)	100.0	4,129
New Zealand	6.2	(0.3)	7.9	(0.3)	27.4	2.1	(0.2)	3.1	(0.2)	47.6	0.8	(0.1)	1.2	(0.1)	50.0	12,790
Northern Ireland	4.1	(0.4)	6.4	(0.4)	56.1	1.9	(0.3)	2.8	(0.3)	47.4	1.0	(0.2)	1.5	(0.2)	50.0	4,340
Poland	0.7	(0.1)	0.9	(0.1)	28.6	0.5	(0.1)	0.5	(0.1)	0.0	0.2	(0.1)	0.3	(0.1)	50.0	10,081
Portugal	4.3	(0.4)	6.1	(0.5)	41.9	2.1	(0.2)	3.3	(0.3)	57.1	0.7	(0.1)	1.1	(0.2)	57.1	3,849
Spain	1.3	(0.2)	1.9	(0.2)	46.2	0.5	(0.1)	0.8	(0.2)	60.0	0.2	(0.1)	0.4	(0.1)	100.0	5,473
Spain (Murcia)	4.7	(0.8)	7.0	(0.9)	48.9	3.0	(0.7)	4.3	(0.7)	43.3	2.1	(0.5)	3.0	(0.6)	42.9	2,621
Netherlands	2.6	(0.4)	3.6	(0.4)	38.5	0.6	(0.2)	1.0	(0.2)	66.7	0.2	(0.1)	0.4	(0.1)	100.0	2,372
United States	5.7	(0.3)	7.8	(0.3)	36.8	2.7	(0.2)	4.0	(0.2)	48.1	1.0	(0.1)	1.6	(0.2)	60.0	9,282
All countries combined	2.7	(0.1)	3.7	(0.1)	37.0	1.2	(0.0)	1.8	(0.1)	50.0	0.5	(0.0)	0.8	(0.0)	60.0	147,261
Comparison between countries^c	F_{28,v} = 76.8*		F_{28,v} = 85.8*			F_{28,v} = 38.8*		F_{28,v} = 42.7*			F_{28,v} = 20.5*		F_{28,v} = 29.0*			
	P < 0.001		P < 0.001			P < 0.001		P < 0.001			P < 0.001		P < 0.001			
Comparison low-, middle-, and high-income country groups^c	F_{2,v} = 253.3*		F_{2,v} = 311.3*			F_{2,v} = 85.0*		F_{2,v} = 106.5*			F_{2,v} = 16.5*		F_{2,v} = 21.7*			
	P < 0.001		P < 0.001			P < 0.001		P < 0.001			P < 0.001		P < 0.001			

Values represent % (SE).

Dashed lines indicate empty cells.

^aAs the numerator and denominator are both zero, a value of 0.0 is shown for per cent change.

^bThe amount of change is greater than zero, but percent change could not be calculated because the denominator is zero.

^cWald design-corrected F-tests were used to determine if there is variation in prevalence estimates across countries. The denominator degree of freedom, v, is 5429.

PRC: People's Republic of China.

prevalence of 2.7%, 12-month prevalence of 1.2%, and 30-day prevalence of 0.5% in the total sample. By contrast, DSM-5 GAD has a lifetime prevalence of 3.7%, an increase of 37% over the rate for DSM-IV GAD. The increases are even larger for recent cases: 12-month prevalence rose to 1.8% (an increase of 50%) and 30-day prevalence rose to 0.8% (an increase of 60%) following the diagnostic revision. Both GAD diagnoses are most prevalent in high-income countries, less prevalent in upper-middle-income countries, and least prevalent in low/lower-middle-income countries. Nevertheless, DSM-5 GAD is more prevalent than DSM-IV GAD in all three country income groups. In fact, with the exception of Nigeria, for which no change was observed, the lifetime prevalence of GAD increased from DSM-IV to DSM-5 in every country examined here.

Comorbidity

Comorbidity also increased from DSM-IV to DSM-5 (Table 6.2). In DSM-IV, more than three-quarters (75.6%) of respondents with lifetime GAD, and more than half (57.1%) of those with 12-month GAD, qualify for at least one other mental disorder assessed by the CIDI. Comorbidity is equally common with mood and anxiety disorders, whether assessed over the respondent's lifetime (50.4% mood vs. 49.2% anxiety) or in the 12 months before interview (33.3% mood vs. 34.5% anxiety); comorbidity is less common with substance-use disorders and least common with disruptive behaviour/impulse-control disorders. Even with the DSM-IV hierarchy rule in effect, MDD is by far the single most common comorbid condition (reported by 42.2% of lifetime DSM-IV GAD cases), followed by social anxiety disorder (25.3%) and specific phobia (24.9%). Interestingly, DSM-IV GAD typically develops later than comorbid disorders: GAD precedes other anxiety disorders in only 12.7% of cases, disruptive behaviour/impulse-control disorders in 33.5% of cases, and mood and substance-use disorders in about 40% of cases.

In DSM-5, rates of comorbidity rose to 81.9% among lifetime cases and to 70.8% among 12-month cases of GAD. As expected, the largest change from DSM-IV is in comorbidity with mood disorders, which are present in the majority of individuals with lifetime (63.0%) and 12-month (51.3%) GAD. Although the number of GAD cases with comorbid MDD far exceeds the number with bipolar spectrum disorder, the percent change in comorbidity is strikingly similar for unipolar and bipolar mood disorders: both increase

by nearly 25% among lifetime GAD cases and by more than 50% among 12-month GAD cases when the hierarchy rule is eliminated. As a result, the proportion of GAD cases with comorbid mood disorders outnumbers the proportion with comorbid anxiety disorders in DSM-5. Nevertheless, rates of comorbid anxiety, substance-use, and disruptive behaviour/impulse-control disorders are all higher for DSM-5 than DSM-IV GAD, suggesting that new cases captured by the revised diagnostic criteria have higher overall levels of comorbidity than previously identified cases. The new cases also disproportionately experience GAD as a temporally secondary disorder. For example, under DSM-5, 75% of respondents with a lifetime history of both GAD and a mood disorder report that GAD began after the mood disorder.

Role Impairment

DSM-5 GAD is associated with greater role impairment than DSM-IV GAD. Respondents with DSM-IV GAD report a mean of 33.9 days (SE = 2.6) out of role due to GAD in the past 12 months, compared to a mean of 41.2 days (SE = 2.4) for those with DSM-5 GAD (data not shown). On the Sheehan Disability Scales, severe functional impairment in one or more life domains is reported by 45.7% of those with DSM-IV GAD versus 50.6% of those with DSM-5 GAD (Table 6.3). Severe impairment is most common in the social domain and least common in the home domain, regardless of GAD definition. In addition, GAD is more disabling in high-income countries than in the upper-middle- or low/lower-middle-income countries under both definitions. Interestingly, although the number of GAD cases with severe impairment increased in all three country income groups in DSM-5, the proportion of severely disabled cases increased more in high- and upper-middle-income countries (11–12% higher than in DSM-IV) than in low/lower-middle-income countries (4% higher than in DSM-IV).

Treatment

DSM-5 GAD is associated with a small but consistent increase in treatment seeking over DSM-IV GAD (Table 6.4). A total of 44.1% of respondents with DSM-IV GAD sought treatment for some type of mental health or substance-use problem during the year before interview, compared to 49.2% of those with DSM-5 GAD. Individuals with GAD, regardless of diagnostic definition, sought treatment most often

Table 6.2 Comorbidity of DSM-IV and DSM-5 generalized anxiety disorder with DSM-IV mental disorders, all countries combined

DSM-IV disorder	DSM-IV			DSM-5		
	Lifetime comorbidity ^a	12-month comorbidity ^b	Temporal priority of GAD ^c	Lifetime comorbidity ^a	12-month comorbidity ^b	Temporal priority of GAD ^c
I. Mood disorder						
Major depressive disorder	42.2 (1.1)	26.8 (1.4)		52.6 (0.9)	40.9 (1.3)	
Bipolar spectrum disorder ^d	9.2 (0.6)	7.0 (0.8)		11.4 (0.6)	10.8 (0.8)	
Any mood disorder ^e	50.4 (1.1)	33.3 (1.5)	40.5 (1.6)	63.0 (0.9)	51.3 (1.3)	24.6 (1.1)
II. Anxiety disorder						
Panic disorder	11.3 (0.8)	8.3 (0.9)		12.3 (0.7)	11.8 (0.9)	
Social anxiety disorder	25.3 (1.0)	18.5 (1.3)		26.1 (0.9)	22.6 (1.2)	
Specific phobia	24.9 (1.0)	22.4 (1.4)		25.6 (0.8)	25.2 (1.2)	
Agoraphobia	8.2 (0.6)	6.5 (0.8)		9.4 (0.5)	9.0 (0.7)	
Posttraumatic stress disorder	18.7 (0.8)	3.7 (0.5)		21.0 (0.7)	14.4 (0.8)	
Childhood-onset separation anxiety disorder ^f	8.9 (0.9)	–		8.6 (0.7)	–	
Adult-onset separation anxiety disorder	13.6 (1.0)	5.7 (0.9)		15.8 (0.8)	6.9 (0.8)	
Any anxiety disorder	49.2 (1.1)	34.5 (1.5)	12.7 (1.0)	51.7 (0.9)	44.0 (1.2)	11.6 (0.8)
III. Disruptive behaviour/Impulse-control disorder						
Intermittent explosive disorder	14.4 (1.3)	11.0 (1.7)		15.0 (1.1)	12.1 (1.4)	
Binge-eating disorder	5.8 (0.7)	3.6 (0.9)		6.1 (0.6)	4.3 (0.8)	
Bulimia nervosa	3.8 (0.5)	1.7 (0.5)		3.8 (0.4)	2.4 (0.5)	
Conduct disorder	8.4 (1.0)	0.3 (0.2)		7.8 (0.8)	1.0 (0.3)	
Attention-deficit/hyperactivity disorder	7.0 (0.8)	4.3 (0.9)		7.5 (0.8)	5.8 (0.9)	
Oppositional defiant disorder	10.7 (1.1)	1.8 (0.6)		10.7 (0.9)	3.5 (0.7)	
Any disruptive behaviour/impulse-control disorder	9.9 (0.7)	7.5 (0.9)	33.5 (2.9)	10.1 (0.6)	8.1 (0.8)	29.8 (2.4)
IV. Substance-use disorder						
Alcohol abuse	19.4 (0.9)	4.6 (0.6)		19.6 (0.8)	5.8 (0.6)	
Alcohol dependence	8.2 (0.6)	3.0 (0.5)		8.9 (0.5)	4.4 (0.6)	
Drug abuse	9.6 (0.7)	2.8 (0.6)		10.5 (0.6)	3.6 (0.6)	
Drug dependence	4.4 (0.4)	1.5 (0.3)		5.3 (0.4)	2.5 (0.5)	
Any substance-use disorder	22.6 (1.0)	7.7 (0.9)	40.3 (2.3)	22.5 (0.8)	9.1 (0.8)	37.2 (1.9)
V. Any mental disorder						
	75.6 (0.9)	57.1 (1.6)	16.0 (1.0)	81.9 (0.7)	70.8 (1.2)	11.0 (0.7)

Values represent % (SE).

^aProportion of respondents with lifetime DSM-IV or DSM-5 GAD who also qualified for the lifetime DSM-IV disorder in each row.

^bProportion of respondents with 12-month DSM-IV or DSM-5 GAD who also qualified for the 12-month DSM-IV disorder in each row.

^cProportion of respondents with lifetime DSM-IV or DSM-5 GAD and at least one disorder in the designated disorder class, whose age-of-onset of GAD is reported to be younger than the age-of-onset of all comorbid disorders in that class.

^dIncludes bipolar I disorder, bipolar II disorder, or subthreshold bipolar disorder.

^eIncludes major depressive episode and bipolar spectrum disorder.

^fThe surveys did not include a 12-month assessment of childhood-onset separation anxiety disorder.

Table 6.3 Severity of role impairment (Sheehan Disability Scale) associated with 12-month DSM-IV and DSM-5 generalized anxiety disorder, by country income group

Proportion with severe role impairment (SDS score: 7-10)	DSM-IV		DSM-5	
	%	SE	%	SE
Home				
Low/lower-middle-income countries	18.9	3.0	23.2	2.8
Upper-middle-income countries	22.2	3.1	25.8	2.2
High-income countries	26.1	1.6	29.4	1.3
All countries combined	24.7	1.3	28.0	1.1
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 2.4$, $P = 0.092$		$F_{2,v} = 2.5$, $P = 0.081$	
Work				
Low/lower-middle-income countries	22.0	3.7	23.7	3.3
Upper-middle-income countries	21.2	3.0	28.7	3.0
High-income countries	29.7	1.7	34.4	1.4
All countries combined	27.4	1.4	32.1	1.2
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 4.0^*$, $P = 0.018$		$F_{2,v} = 5.4^*$, $P = 0.005$	
Relationship				
Low/lower-middle-income countries	24.7	4.5	26.1	3.4
Upper-middle-income countries	23.6	2.8	26.8	2.2
High-income countries	27.6	1.6	33.0	1.3
All countries combined	26.6	1.4	31.1	1.1
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 0.9$, $P = 0.427$		$F_{2,v} = 4.1^*$, $P = 0.016$	
Social				
Low/lower-middle-income countries	27.3	4.7	24.6	3.7
Upper-middle-income countries	24.2	2.9	28.4	2.8
High-income countries	32.8	1.8	38.1	1.4
All countries combined	30.7	1.5	34.9	1.2
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 3.2^*$, $P = 0.039$		$F_{2,v} = 9.6^*$, $P < 0.001$	
Any^b				
Low/lower-middle-income countries	37.5	4.7	39.0	3.6
Upper-middle-income countries	38.1	3.4	42.6	3.0
High-income countries	49.0	1.8	54.5	1.4
All countries combined	45.7	1.5	50.6	1.2
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 5.8^*$, $P = 0.003$		$F_{2,v} = 13.0^*$, $P < 0.001$	

*Significant at the 0.05 level, two-sided test.

^aWald design-corrected F-tests were used to determine if there is variation in impairment severity across country income groups. The denominator degree of freedom, v , is 5429.

^bHighest severity category across the four SDS role domains.

in general medical settings, less often in specialty mental health settings, and very rarely in human services or complementary-alternative settings. Help-seeking patterns differ greatly by country income, with very few GAD cases by either definition receiving specialty mental health treatment in low /lower-middle-income countries, and with a far higher rate of treatment overall in high-income than upper-middle- or low/lower-middle-income countries. Despite these broader patterns, treatment seeking is higher for DSM-5 than DSM-IV GAD in all three country income groups.

Course and Correlates

DSM-IV and DSM-5 GAD have a similar course of illness. Median age-of-onset (AOO) (ages 38 and 39 for DSM-IV and DSM-5 GAD, respectively) and cumulative AOO distributions are nearly identical for the two diagnoses (Table 6.5). GAD typically begins after puberty: only 5% of cases develop by age 13. New cases emerge gradually through adolescence and adulthood, with one-quarter of GAD cases beginning by ages 24–25, half

Table 6.4 Among those with 12-month DSM-IV and DSM-5 generalized anxiety disorder, percent reporting treatment in the past 12 months

Sector of treatment	DSM-IV		DSM-5	
	%	SE	%	SE
Specialty mental health^b				
Low/lower-middle-income countries	1.3	0.6	3.7	1.4
Upper-middle-income countries	12.0	2.1	16.5	2.3
High-income countries	27.4	1.7	32.3	1.3
All countries combined	21.6	1.3	26.0	1.1
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 55.2^*$, $P < 0.001$		$F_{2,v} = 72.1^*$, $P < 0.001$	
General medical^c				
Low/lower-middle-income countries	11.5	2.9	11.4	2.2
Upper-middle-income countries	13.6	2.1	14.7	2.0
High-income countries	37.2	1.7	41.0	1.4
All countries combined	29.9	1.3	32.8	1.1
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 42.5^*$, $P < 0.001$		$F_{2,v} = 76.8^*$, $P < 0.001$	
Human services^d				
Low/lower-middle-income countries	5.1	2.8	6.4	2.2
Upper-middle-income countries	3.0	1.1	3.8	1.0
High-income countries	6.4	1.0	7.6	0.8
All countries combined	5.6	0.8	6.8	0.6
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 2.6$, $P = 0.08$		$F_{2,v} = 4.7^*$, $P = 0.01$	
Complementary-alternative medicine^e				
Low/lower-middle-income countries	3.1	1.4	2.4	0.9
Upper-middle-income countries	2.5	1.0	4.0	1.5
High-income countries	7.2	0.8	8.2	0.8
All countries combined	5.9	0.6	6.8	0.1
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 7.4^*$, $P < 0.001$		$F_{2,v} = 12.0^*$, $P < 0.001$	
Any treatment^f				
Low/lower-middle-income countries	19.6	4.1	21.7	3.3
Upper-middle-income countries	24.5	2.9	29.1	2.8
High-income countries	53.3	1.6	59.0	1.3
All countries combined	44.1	1.4	49.2	1.2
Comparison between low-, middle-, and high-income countries^a	$F_{2,v} = 45.3^*$, $P < 0.001$		$F_{2,v} = 73.6^*$, $P < 0.001$	

*Significant at the 0.05 level, two-sided test.

^aWald design-corrected F-tests were used to determine if there is variation in treatment estimates across country income groups. The denominator degree of freedom, v , is 5429.

^bThe mental health specialist sector, which includes psychiatrist and non-psychiatrist mental health specialists (psychiatrist, psychologist or other non-psychiatrist mental health professional; social worker or counsellor in a mental health specialty setting; use of a mental health helpline; or overnight admissions for a mental health or drug or alcohol problems, with a presumption of daily contact with a psychiatrist).

^cThe general medical sector (general practitioner, other medical doctor, nurse, occupational therapist or any healthcare professional).

^dThe human services sector (religious or spiritual advisor or social worker or counsellor in any setting other than a specialty mental health setting).

^eThe CAM (complementary and alternative medicine) sector (any other type of healer, such as herbalist or homeopath, participation in an internet support group, or participation in a self-help group).

^fAny treatment listed above.

beginning by ages 38–39, and three-quarters beginning by age 53. Only 10% of first onsets occur in adults aged 65 or older. Once GAD begins, it often persists: 44.8% of individuals with DSM-IV GAD and 48.8% of individuals with DSM-5 GAD in their

lifetime still had the disorder in the year before interview. Onsets are somewhat earlier and course is less persistent in high-income countries than in upper-middle- or low/lower-middle-income countries for both GAD diagnoses (data not shown).

Table 6.5 Cumulative age-of-onset distributions for DSM-IV and DSM-5 generalized anxiety disorder (GAD), by country income group

DSM edition	Ages at selected percentiles								Projected risk at age 75 % (SE)
	5	10	25	50	75	90	95	99	
DSM-IV									
Low/lower-middle-income countries	14	18	28	44	56	70	70	74	2.6 (0.4)
Upper-middle-income countries	14	18	29	44	64	72	73	73	5.1 (0.6)
High-income countries	12	14	22	35	50	60	67	73	6.0 (0.2)
All countries combined	13	15	24	38	53	65	71	73	5.1 (0.2)
DSM-5									
Low/lower-middle-income countries	15	18	28	43	56	66	70	74	3.7 (0.4)
Upper-middle-income countries	14	18	29	43	62	72	72	73	6.7 (0.6)
High-income countries	13	14	23	36	50	61	68	74	8.7 (0.4)
All countries combined	13	16	25	39	53	65	70	74	7.3 (0.3)

Values represent ages at selected percentiles on the standardized age-of-onset (AOO) distributions for DSM-IV and DSM-5 GAD. These values, and the projected lifetime risk of GAD at age 75, are based on survival models.

DSM-IV and DSM-5 GAD also have very similar socio-demographic correlates (Table 6.6). Both lifetime diagnoses are more prevalent among young (under age 60), female, and previously married individuals. Both are also more prevalent among individuals with less education, a lower household income, and 'other' employment status (mostly unemployed or disabled), although these three variables are consistently associated with GAD only in high-income countries. Socio-demographic correlates of 30-day GAD are also very similar regardless of how the disorder was defined. Where correlates for 30-day GAD deviate from the profile for lifetime cases (e.g., weaker associations with age; elevated odds among homemakers as well as those of 'other' employment status), the deviations are evident for both DSM-IV and DSM-5 GAD. In spite of these similarities, the associations with socio-demographic variables generally are a bit larger, show a clearer dose-response gradient, and are more consistent across lifetime and 30-day analyses for DSM-5 than DSM-IV GAD. Likewise, socio-demographic predictors of course (disorder persistence) are similar for the two diagnoses, but slightly more robust for DSM-5 GAD. Neither female gender nor previously married status is associated with a more persistent course of illness. Instead, GAD is more persistent among individuals with an earlier onset of GAD, lower education and family income, and – for DSM-5 GAD – lack of employment outside the home ('other' status or homemaker).

Discussion

The challenge of separating clinically significant anxiety from normal anxiety and from other forms of emotional disturbance has spurred repeated revisions of the definition of GAD. The decision in DSM-5 to remove GAD's hierarchical relationship with the mood disorders raises new opportunities for understanding GAD and describing its connections to other disorders. In this chapter we examined the implications of this decision for the epidemiology of GAD in a large, multinational sample. Eliminating the hierarchy rule led to an influx of new GAD cases: prevalence estimates increased by 37% for lifetime GAD, by 50% for 12-month GAD, and by 60% for 30-day GAD compared to DSM-IV estimates in the same surveys. Notably, the prevalence estimates reported here for the broadened DSM-5 diagnosis are still lower than those published for DSM-IV GAD in reviews of previous epidemiological surveys (Somers *et al.* 2006). This appears to be due mainly to the lower prevalence of GAD in low/lower-middle-income countries, which were excluded from earlier reviews. Our results highlight the importance of studying GAD in developing as well as developed countries, given reliable differences not only in prevalence but also in degree of role impairment, patterns of treatment seeking, and course of illness across country groups (see also Ruscio *et al.* 2017). At the same time, the results show consistently that DSM-5 GAD is more prevalent and severe than DSM-IV GAD across countries, irrespective of

Table 6.6 Bivariate associations of socio-demographic correlates with DSM-IV and DSM-5 generalized anxiety disorder (GAD), all countries combined

Variable	DSM-IV						DSM-5					
	Lifetime GAD ^a		30-day GAD ^b		12-month GAD, lifetime cases ^c		Lifetime GAD ^a		30-day GAD ^b		12-month GAD/ lifetime cases ^c	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Age-cohort												
18–29	4.8*	(4.0–5.7)	0.9	(0.7–1.2)	–	–	6.0*	(5.1–7.0)	0.9	(0.7–1.2)	–	–
30–44	4.0*	(3.5–4.5)	1.2	(1.0–1.6)	–	–	4.8*	(4.3–5.4)	1.4*	(1.1–1.6)	–	–
45–59	2.6*	(2.3–2.9)	1.3	(1.0–1.6)	–	–	3.0*	(2.7–3.3)	1.4*	(1.2–1.8)	–	–
60+	1.0		1.0		–	–	1.0		1.0		–	–
χ^2 (P Value) ^d	445.2	(<0.001)	10.9	(0.012)	–	–	743.8	(<0.001)	32.1	(<0.001)	–	–
Age-of-onset												
Early	–		–		1.7*	(1.3–2.3)	–	–	–		1.8*	(1.5–2.3)
Early-average	–		–		1.4*	(1.1–1.7)	–	–	–		1.2*	(1.0–1.5)
Late-average	–		–		1.1	(0.8–1.3)	–	–	–		1.0	(0.8–1.2)
Late	–		–		1.0		–	–	–		1.0	
χ^2 (P Value) ^d	–		–		20.8	(<0.001)	–	–	–		45.9	(<0.001)
Gender												
Female	1.7*	(1.6–1.9)	1.8*	(1.5–2.2)	1.1	(0.9–1.3)	1.8*	(1.7–2.0)	1.9*	(1.6–2.3)	1.1	(0.9–1.3)
Male	1.0		1.0		1.0		1.0		1.0		1.0	
χ^2 (P Value) ^d	196.9	(<0.001)	32.8	(<0.001)	1.1	(0.306)	313.2	(<0.001)	53.5	(<0.001)	1.3	(0.249)
Marital status												
Never married	1.1	(1.0–1.2)	0.8	(0.6–1.0)	0.9	(0.8–1.2)	1.2*	(1.1–1.3)	0.9	(0.7–1.0)	1.1	(0.9–1.3)
Divorced/separated/widowed	1.5*	(1.3–1.6)	1.5*	(1.2–1.8)	1.0	(0.8–1.2)	1.6*	(1.5–1.8)	1.7*	(1.4–2.0)	1.1	(0.9–1.3)
Currently married	1.0		1.0		1.0		1.0		1.0		1.0	
χ^2 (P Value) ^d	59.4	(<0.001)	12.3	(0.002)	0.3	(0.871)	131.4	(<0.001)	33.4	(<0.001)	1.0	(0.604)
Education level												
No education	1.7*	(1.3–2.3)	3.0*	(1.8–5.2)	1.5	(0.8–2.7)	1.8*	(1.4–2.3)	3.1*	(2.0–4.8)	1.4	(0.8–2.3)
Some primary	1.4*	(1.2–1.7)	2.1*	(1.4–3.0)	1.7*	(1.2–2.4)	1.4*	(1.2–1.6)	2.1*	(1.6–2.9)	1.9*	(1.4–2.5)
Finished primary	1.5*	(1.3–1.8)	2.2*	(1.5–3.3)	1.8*	(1.2–2.7)	1.6*	(1.3–1.8)	2.4*	(1.7–3.3)	1.7*	(1.2–2.3)
Some secondary	1.3*	(1.2–1.5)	1.8*	(1.3–2.4)	1.4*	(1.1–1.8)	1.4*	(1.3–1.6)	2.1*	(1.6–2.6)	1.5*	(1.2–1.8)
Finished secondary	1.2*	(1.1–1.4)	1.3	(0.9–1.8)	1.4*	(1.1–1.8)	1.2*	(1.1–1.4)	1.5*	(1.1–1.9)	1.3*	(1.0–1.6)
Some college	1.2*	(1.0–1.3)	1.2	(0.9–1.6)	1.1	(0.9–1.4)	1.3*	(1.1–1.4)	1.4*	(1.1–1.8)	1.1	(0.9–1.4)
Finished college	1.0		1.0		1.0		1.0		1.0		1.0	
χ^2 (P Value) ^d	35.6	(<0.001)	36.4	(<0.001)	16.5	(0.011)	54.1	(<0.001)	58.6	(<0.001)	24.2	(0.001)

(cont.)

Section II: The Disorders

Table 6.6 (cont.)

Variable	DSM-IV						DSM-5					
	Lifetime GAD ^a		30-day GAD ^b		12-month GAD, lifetime cases ^c		Lifetime GAD ^a		30-day GAD ^b		12-month GAD/ lifetime cases ^c	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Household income												
Low	1.2*	(1.1–1.3)	1.4*	(1.1–1.8)	1.4*	(1.1–1.8)	1.3*	(1.1–1.4)	1.7*	(1.4–2.1)	1.6*	(1.3–2.0)
Low-average	1.1	(1.0–1.3)	1.2	(1.0–1.6)	1.3*	(1.0–1.6)	1.2*	(1.0–1.3)	1.3*	(1.0–1.6)	1.4*	(1.1–1.7)
High-average	1.1*	(1.0–1.3)	1.2	(0.9–1.6)	1.4*	(1.1–1.7)	1.1*	(1.0–1.3)	1.2	(1.0–1.5)	1.3*	(1.1–1.6)
High	1.0		1.0		1.0		1.0		1.0		1.0	
χ^2 (P Value) ^d	8.1	(0.045)	6.5	(0.089)	9.0	(0.029)	20.8	(<0.001)	24.8	(<0.001)	22.1	(<0.001)
Employment status												
Student	1.0	(0.8–1.3)	0.9	(0.6–1.5)	1.3	(0.8–2.1)	1.2	(0.9–1.5)	1.1	(0.7–1.7)	1.5	(1.0–2.4)
Homemaker	1.1	(0.9–1.2)	1.5*	(1.1–2.0)	1.1	(0.9–1.4)	1.1	(1.0–1.2)	1.5*	(1.2–1.9)	1.2*	(1.0–1.5)
Retired	0.9*	(0.7–1.0)	0.9	(0.6–1.2)	1.2	(0.9–1.6)	0.9	(0.8–1.0)	0.8	(0.7–1.1)	1.2	(1.0–1.5)
Other	1.6*	(1.4–1.8)	2.2*	(1.8–2.8)	1.3	(1.0–1.6)	1.7*	(1.5–1.9)	2.4*	(2.0–2.9)	1.6*	(1.3–2.0)
Employed	1.0		1.0		1.0		1.0		1.0		1.0	
χ^2 (P Value) ^d	64.6	(<0.001)	51.3	(<0.001)	5.2	(0.272)	113.3	(<0.001)	81.1	(<0.001)	22.7	(<0.001)

*Significant at the 0.05 level, two-sided test.

Dashed lines indicate empty cells.

^aBased on survival models adjusted for age-cohorts, gender, person-years, and country. The denominator used for these estimates is the number of person-years in the survival models (N = 6,383,860 for DSM-IV models; N = 6,360,664 for DSM-5 models).

^bBased on logistic regression models adjusted for age, gender, and country. The denominator used for these estimates is the number of respondents in the total sample (N = 147,261).

^cBased on logistic regression models predicting 12-month GAD among lifetime cases, adjusted for time since GAD onset, age of GAD onset, sex, and country. The denominator used for these estimates is the number of lifetime GAD cases (N = 4,262 for DSM-IV models; N = 5,888 for DSM-5 models).

^dChi-square test of significant differences between blocks of socio-demographic variables.

economic development. This provides some assurance that the consequences of the latest GAD revision generalize to many parts of the world in which the DSM is used to inform research, policy, and clinical care.

The diagnostic revision led to several alterations in the epidemiology of GAD, suggesting that new cases captured by the revised criteria differ in meaningful ways from cases identified using DSM-IV criteria. Not surprisingly, some of the most notable differences concerned rates and patterns of comorbidity with other disorders. Approximately 82% of individuals with lifetime DSM-5 GAD qualified for another lifetime disorder, a small increase from the 76% comorbidity estimate for DSM-IV GAD. The increase in comorbidity was more striking among 12-month GAD cases, with more than 70% qualifying for another 12-month disorder under DSM-5 compared to 57% under DSM-IV. Although an increase in comorbidity was expected, the relatively larger increase in comorbidity among 12-month cases than lifetime cases warrants some consideration. A possible methodological explanation is that better memory for recent than distant disorders contributed to increased reporting of comorbid disorders, including hierarchy-triggering mood disorders, in the past year (i.e., a recall effect); another possibility is that lifetime comorbidity rates were already so high for DSM-IV GAD that there was relatively little room for comorbidity to increase under DSM-5 (i.e., a ceiling effect). An alternative, more substantive explanation is that individuals with chronic GAD may be more highly concentrated among 12-month cases than among lifetime cases, who include previously remitted cases as well as those whose GAD persisted without remission. There is some evidence that having a comorbid disorder predicts an unremitting course of GAD (Bruce *et al.* 2001). Additionally, unremitting GAD may be a marker of greater clinical severity or of exposure to risk factors that are particularly severe (e.g., strong genetic diathesis) or enduring (e.g., chronic stress), which may themselves increase the likelihood of comorbidity.

Predictably, the most significant change in comorbidity occurred with mood disorders. Even with the DSM-IV hierarchy rule in effect, comorbid MDD was present in more than 40% of lifetime GAD cases. When the hierarchy rule was lifted, comorbidity increased to more than 50%. The increase was even more dramatic among respondents who experienced GAD in the past year, of whom just over one-quarter were in a major depressive episode in the past year under DSM-IV compared to more than 40% under DSM-5. Based on trends

observed in previous research (Ruscio & Khazanov 2017), comorbidity rates are likely to be even higher in clinical samples. Nevertheless, the finding that about half of people with lifetime DSM-5 GAD have never had MDD appears to support the continued separation of these disorders (Goldberg *et al.* 2010).

Although our analyses did not directly address the question of whether GAD should be considered an anxiety disorder or depressive disorder, the results do offer some relevant insights. Whereas DSM-IV GAD had roughly equal rates of lifetime comorbidity with mood disorders and other anxiety disorders (50% versus 49%), DSM-5 GAD had higher comorbidity with mood than anxiety disorders (63% versus 52%). Notably, this deviates from the pattern of substantially higher comorbidity with anxiety than mood disorders that was observed for every other anxiety disorder in the WMH surveys except posttraumatic stress disorder, which in DSM-5 is no longer classified as an anxiety disorder (see Chapters 7–12 in this volume). DSM-5 GAD also resembles MDD more closely than other anxiety disorders in these surveys in having a fairly late AOO, slow accumulation of new cases across the lifespan, and relatively less persistent course of illness. These epidemiological results are consistent with results from large factor analytic studies (Krueger 1999; Watson 2005) suggesting a closer relationship of GAD with depressive disorders than with other anxiety disorders. Although the collective findings appear to support a departure of GAD from the family of anxiety disorders, other considerations may support its continued classification with these disorders. For example, in prospective research, psychosocial risk factors for GAD have been shown to align more closely with those for anxiety disorders than depressive disorders (Beesdo *et al.* 2010). From a more pragmatic standpoint, focusing on GAD's prominent anxiety symptoms may help promote clinical detection and accurate diagnosis of the disorder – an important consideration given that GAD remains poorly recognized, especially in general medical settings (Wittchen *et al.* 2002).

Of note, the new cases identified by DSM-5 disproportionately reported that their GAD began after the onset of another mental disorder. This diverges from conventional clinical wisdom which dictates that anxiety typically precedes depression, as well as from prior research which documented a nearly equal number of comorbid cases beginning with GAD versus MDD (Moffitt *et al.* 2007). Our research suggests that once the hierarchy rule is lifted, an imbalance emerges, with

mood disorders (typically MDD) tending to onset before GAD. One explanation for this may be methodological; by definition, GAD cases that emerged first would not meet the hierarchy rule and would be diagnosed by the DSM-IV criteria. Nevertheless, substantive interpretations are also possible. For example, GAD may be a complication of, or a reaction to, a major depressive episode, such as when role impairments associated with depression create secondary problems (e.g., job loss, poor grades, relationship strain) that elicit anxiety. A different possibility, consistent with the idea that anxiety precedes depression, is that the propensity to worry emerges early in life but may not be recognized as a problem until a major stressor – or perhaps another disorder – undermines the ability to manage worry successfully. Research collecting more detailed information about the onset of worry as well as GAD, and about the environmental contexts in which GAD and other disorders first emerge, would aid in understanding the causes of GAD and the functional relationships between disorders that could be targeted in treatment.

Several aspects of the GAD diagnosis, including socio-demographic correlates and AOO, remained stable irrespective of the criterion set applied. Consistent with previous epidemiological research (Grant *et al.* 2005; Lieb *et al.* 2005), individuals with GAD were more likely to be young (below age 60), female, and previously married (divorced, separated, or widowed). In high-income countries, GAD was also associated with lower education, lower income, and a lack of full-time employment. These similarities suggest that GAD is fundamentally the same disorder, concentrated in the same segments of the population, under the two diagnostic definitions. At the same time, DSM-5 cases tended to report more significant role impairment due to GAD, especially in upper-middle- and high-income countries, and were correspondingly more likely to seek treatment. Taken together, these results suggest that the revised criteria were successful in capturing clinically significant cases of GAD that were missed by the DSM-IV diagnosis. The greater severity of these cases is consistent with prior studies, which found greater psychopathology (Zimmerman & Chelminski 2003; Lawrence *et al.* 2009) and a more adverse risk profile (Moffitt *et al.* 2007) among comorbid relative to ‘pure’ GAD and MDD. Importantly, the available findings do not resolve whether the new cases actually involve multiple, distinct disorders (e.g., comorbid GAD and MDD) or a severe form of mood disorder (e.g., an

anxious subtype of MDD); these and another possibilities await evaluation using methods appropriate for explicating comorbidity (Klein & Riso 1993; Neale & Kendler 1995; J. Ruscio & Ruscio 2004). Nevertheless, the observed severity underscores the importance of recognizing the significant consequences of co-occurring anxiety in these former hierarchy cases, especially as the presence of comorbid GAD may have implications for treatment (Zimmerman & Chelminski 2003; Coplan *et al.* 2015).

A notable strength of the current study is the large, multinational sample that was representative of the household populations in the countries and regions included here. The large sample size allowed for the detection of subtle changes from DSM-IV to DSM-5 GAD and increased confidence in the reliability of the findings. The use of representative community samples ensured that results were not biased by self-selection into treatment or by features of specific clinical sites. The inclusion of 29 surveys from 26 diverse countries ensured that results were not limited to particular regions, cultures, or strata of economic development. Nevertheless, the study also had several limitations. Perhaps most important, GAD diagnoses were assigned based on fully structured interviews administered by lay interviewers. Although the CIDI shows good concordance with the SCID, it is possible that results would have differed if diagnoses had been assigned by expert clinicians. This is a particular concern given the challenges of differentiating GAD from MDD symptoms and establishing the dates of episode onset and remission, even for experienced clinicians. Another limitation is that symptom onset was assessed retrospectively; consequently, some caution is warranted when interpreting the AOO and temporal priority data. The timing of GAD and mood disorders was determined from these AOO reports along with reports of symptom offset and episode duration, which were rounded to the nearest year and dated separately for each disorder. Consequently, in the common situation of two disorders beginning in the same year (Kessler *et al.* 2008), we were unable to distinguish simultaneous onsets from onsets that were separated within the year. Finally, although considerable effort was made to standardize data collection across surveys, cultural variation in the interpretation of concepts such as ‘excessive worry’ and ‘feeling sad, empty, or depressed’ may have contributed to cross-national differences.

This chapter presents the first comparison of DSM-IV and DSM-5 GAD in the general population. In

a large, multinational sample, lifting the DSM-IV hierarchy with mood disorders increased the prevalence of GAD substantially. The newly identified GAD cases appeared to be more severe than previously identified cases on several dimensions. DSM-5 GAD was associated with somewhat higher rates of role impairment and treatment seeking than DSM-IV GAD. In addition, DSM-5 GAD was associated more strongly with psychiatric comorbidity in general and MDD comorbidity in particular, with most GAD onsets occurring after the onset of another mental disorder. These patterns of comorbidity are consistent with findings from empirically derived taxonomies, which tend to group GAD with depressive disorders rather than anxiety disorders. Other important correlates of GAD such as female gender, previously married status, lower education and income, and a lack of full-time employment remained unchanged. Whether DSM-IV or DSM-5 criteria are applied, these findings converge on a conceptualization of GAD as a common disorder that is associated with considerable morbidity and disability.

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References

- Abel, J. L. & Borkovec, T. D. (1995). Generalizability of DSM-III-R generalized anxiety disorders to proposed DSM-IV criteria and cross-validation of proposed changes. *Journal of Anxiety Disorders*, 4, 303–15.
- American Psychiatric Association. (1980). *Diagnostic and Statistical Manual of Mental Disorders*. 3rd ed. Washington, DC: Author.
- (1987). *Diagnostic and Statistical Manual of Mental Disorders*. 3rd ed., revised. Washington, DC: Author.
- (1994). *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: Author.
- (2013). *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC: Author.
- Andrews, G., Hobbs, M. J., Borkovec, T. D., et al. (2010). Generalized worry disorder: a review of DSM-IV generalized anxiety disorder and options for DSM-V. *Depression and Anxiety*, 27, 134–47.
- Ballenger, J. C., Davidson, J., Lecrubier, Y., & Wittchen, H. U. (2001). Consensus statement on generalized anxiety disorder from the International Consensus Group on Depression and Anxiety. *The Journal of Clinical Psychiatry*, 62, 53–8.
- Beesdo, K., Pine, D. S., Lieb, R., & Wittchen, H. U. (2010). Incidence and risk patterns of anxiety and depressive disorders and categorization of generalized anxiety disorder. *Archives of General Psychiatry*, 67, 47–57.
- Berkson, J. (1946). Limitations of the application of the four-fold table analysis to hospital data. *Biometrics Bulletin*, 2, 47–53.
- Brown, T. A., Barlow, D. H., & Liebowitz, M. R. (1994). The empirical basis of generalized anxiety disorder. *American Journal of Psychiatry*, 151, 1272–80.
- Brown, T. A., DiNardo, P. A., Lehman, C. L., & Campbell, L. A. (2001). Reliability of DSM-IV anxiety and mood disorders: implications for the classification of emotional disorders. *Journal of Abnormal Psychology*, 110, 49–58.
- Bruce, S. E., Machan, J. T., Dyck, I., & Keller, M. B. (2001). Infrequency of “pure” GAD: impact of psychiatric comorbidity on clinical course. *Depression and Anxiety*, 14, 219–25.
- Chelminski, I. & Zimmerman, M. (2003). Pathological worry in depressed and anxious patients. *Journal of Anxiety Disorders*, 17, 553–46.
- Coplan, J. D., Aaronson, C. J., Panthangi, V., & Kim, Y. (2015). Treating comorbid anxiety and depression: psychosocial and pharmacological approaches. *World Journal of Psychiatry*, 5, 366–78.
- Davidson, J. R., Zhang, W., Connor, K. M., et al. (2010). A psychopharmacological treatment algorithm for generalised anxiety disorder (GAD). *Journal of Psychopharmacology*, 24, 3–26.
- Ehring, T. & Watkins, E. R. (2008). Repetitive negative thinking as a transdiagnostic process. *International Journal of Cognitive Therapy*, 1, 192–205.
- First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2002). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders: Research Version, Non-patient Ed.* New York, NY: Biometrics Research, New York State Psychiatric Institute.
- Goldberg, D., Kendler, K. S., Sirovatka, P. J., & Regier, D. A., eds. (2010). *Diagnostic Issues in Depression and Generalized Anxiety Disorder: Refining the Research Agenda for DSM-V*. Washington, DC: American Psychiatric Association.
- Grant, B. F., Hasin, D. S., Stinson, F. S., et al. (2005). Prevalence, correlates, co-morbidity, and comparative disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychological Medicine*, 35, 1747–59.
- Haro, J. M., Arbabzadeh-Bouchez, S., Brugha, T. S., et al. (2006). Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health Surveys. *International Journal of Methods in Psychiatric Research*, 15, 167–80.
- Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1992). Major depression and generalized

- anxiety disorder: same genes, (partly) different environments? *Archives of General Psychiatry*, 49, 716–22.
- Kessler, R. C., Gruber, M., Hettema, J. M., Hwang, I., Sampson, N., & Yonkers, K. A. (2008). Comorbid major depression and generalized anxiety disorders in the National Comorbidity Survey follow-up. *Psychological Medicine*, 38, 365–74.
- Klein, D. N., & Riso, L. P. (1993). Psychiatric disorders: Problems of boundaries and comorbidity. In C. G. Costello (Ed.), *Basic Issues in Psychopathology* (pp. 19–66). New York, NY: Guilford Press.
- Krueger, R. F. (1999). The structure of common mental disorders. *Archives of General Psychiatry*, 56, 921–6.
- Lawrence, A. E., Liverant, G. I., Rosellini, A. J., & Brown, T. A. (2009). Generalized anxiety disorder within the course of major depressive disorder: examining the utility of the DSM-IV hierarchy rule. *Depression and Anxiety*, 26, 909–16.
- Lewis-Fernández, R., Hinton, D. E., Laria, A. J., et al. (2010). Culture and the anxiety disorders: recommendations for DSM-V. *Depression and Anxiety*, 27, 212–29.
- Lieb, R., Becker, E., & Altamura, C. (2005). The epidemiology of generalized anxiety disorder in Europe. *European Neuropsychopharmacology*, 15, 445–52.
- Marten, P. A., Brown, T. A., Barlow, D. H., Borkovec, T. D., Shear, M. K., & Lydiard, R. B. (1993). Evaluation of the ratings comprising the associated symptom criterion of DSM-III-R generalized anxiety disorder. *Journal of Nervous and Mental Disease*, 181, 676–82.
- Merikangas, K. R., Akiskal, H. S., Angst, J., et al. (2007). Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, 64, 543–52.
- Moffitt, T. E., Caspi, A., Harrington, H., et al. (2007). Generalized anxiety disorder and depression: childhood risk factors in a birth cohort followed to age 32. *Psychological Medicine*, 37, 441–52.
- Moffitt, T. E., Harrington, H., Caspi, A., et al. (2007). Depression and generalized anxiety disorder: cumulative and sequential comorbidity in a birth cohort followed prospectively to age 32 years. *Archives of General Psychiatry*, 64, 651–60.
- Neale, M. C., & Kendler, K. S. (1995). Models of comorbidity for multifactorial disorders. *American Journal of Human Genetics*, 57, 935–53.
- Rickels, K. & Rynn, M. (2001). Overview and clinical presentation of generalized anxiety disorder. *Psychiatric Clinics of North America*, 24, 1–17.
- Ruscio, A. M., Hallion, L. S., Lim, C. C. W., et al. (2017). Cross-sectional comparison of the epidemiology of DSM-5 generalized anxiety disorder across the globe. *JAMA Psychiatry*, 74, 465–75.
- Ruscio, A. M. & Khazanov, G. K. (2017). Anxiety and depression. In R. J. DeRubeis and D. R. Strunk (eds.), *Oxford Handbook of Mood Disorders* (pp. 313–24). New York, NY: Oxford University Press.
- Ruscio, A. M., Lane, M., Roy-Byrne, P., et al. (2005). Should excessive worry be required for a diagnosis of generalized anxiety disorder? Results from the US National Comorbidity Survey Replication. *Psychological Medicine*, 35, 1761–772.
- Ruscio, J., & Ruscio, A. M. (2004). Clarifying boundary issues in psychopathology: the role of taxometrics in a comprehensive program of structural research. *Journal of Abnormal Psychology*, 113, 24–38.
- Somers, J. M., Goldner, E. M., Waraich, P., & Hsu, L. (2006). Prevalence and incidence studies of anxiety disorders: a systematic review of the literature. *The Canadian Journal of Psychiatry*, 51, 100–13.
- Starcevic, V., Portman, M. E., & Beck, A. T. (2012). Generalized anxiety disorder: between neglect and an epidemic. *Journal of Nervous and Mental Disease*, 200, 664–7.
- The World Bank. (2009). *Data & Statistics, Country Groups by Income*. Retrieved from <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519>.
- Watson, D. (2005). Rethinking the mood and anxiety disorders: A quantitative hierarchical model for DSM-V. *Journal of Abnormal Psychology*, 114, 522–36.
- (2009). Differentiating the mood and anxiety disorders: A quadripartite model. *Annual Review of Clinical Psychology*, 5, 221–47.
- Wittchen, H. U., Kessler, R. C., Beesdo, K., Krause, P., Höfler, M., & Hoyer, J. (2002). Generalized anxiety and depression in primary care: Prevalence, recognition, and management. *The Journal of Clinical Psychiatry*, 63, 24–34.
- Zimmerman, M. & Chelminski, I. (2003). Generalized anxiety disorder in patients with major depression: is DSM-IV's hierarchy correct? *American Journal of Psychiatry*, 160, 504–12.