

# Broadening the definition of generalized anxiety disorder: Effects on prevalence and associations with other disorders in the National Comorbidity Survey Replication

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## Abstract

Concerns have been raised that the DSM-IV requirements of 6-month duration, excessive worry, and three associated symptoms exclude a substantial number of people with clinically significant anxiety from a diagnosis of generalized anxiety disorder (GAD). We examined the implications of relaxing these three criteria for the estimated prevalence and predictive validity of GAD using nationally representative data from the US National Comorbidity Survey Replication. Relaxing all three criteria more than doubles the estimated prevalence of GAD. Broadly defined GAD significantly predicts the subsequent first onset of a wide range of temporally secondary disorders. The odds of secondary disorders are somewhat smaller for broadly defined than DSM-IV GAD, though few of these differences are statistically significant. Results suggest that subthreshold manifestations of GAD are significantly related to elevated risk of subsequent psychopathology. Further research is needed to determine whether broadening the current diagnostic criteria results in a more valid characterization of GAD.

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The diagnostic definition of generalized anxiety disorder (GAD) has been a source of debate since the disorder was first introduced in the third edition of the *Diagnostic and Statistical Manual of Mental disorders (DSM-III)* (American Psychiatric Association, 1980). Given the challenges of distinguishing generalized anxiety from normal stress reactions and from other anxiety and mood disorders (Barlow, Blanchard, Vermilyea, Vermilyea, & DiNardo, 1986; Breslau & Davis, 1985; Brown, Barlow, & Liebowitz, 1994), it is perhaps not surprising that the definition of GAD has changed substantially with each subsequent DSM revision. DSM-III defined GAD as 1 month of persistent anxiety accompanied by associated symptoms from three of four categories. DSM-III-R changed the requirements to 6 months of worry along with 6 of 18 associated symptoms to improve the validity of separation from normal anxiety and from anxiety that occurs secondary to other mental disorders (American Psychiatric Association, 1987). DSM-IV made further changes aimed at sharpening the characterization of GAD by requiring that worry be excessive and uncontrollable (American Psychiatric Association, 1994). DSM-IV also stipulated that the worry in GAD must be associated with at least three of six symptoms of tension and vigilance, and cause significant distress or impairment.

Although these changes have led to improved reliability of GAD diagnoses (Brown, Di Nardo, Lehman, & Campbell, 2001), debates persist about validity. Research has found that GAD lasting at least 1 month has very similar socio-demographic and clinical correlates (Kessler et al., 2005b) and is at least as heritable (Kessler, Neale, Kessler, Heath, & Eaves, 1992) as GAD lasting 6 or more months, consistent with views of GAD as a chronic-recurrent condition that may manifest as brief, repeated episodes (Rickels & Rynn, 2001). Individuals who do not view their worry as excessive, but who meet all other DSM-IV GAD criteria, have been found to suffer substantial anxiety and report functional impairment, treatment seeking, and parental GAD at levels comparable to excessive worriers (Ruscio et al., 2005), seeming to support the omission of excessiveness from the ICD-10 (*International Classification of Diseases*, 10th ed.) (World Health Organization, 1993) definition of GAD. While growing evidence supports the narrowed DSM-IV focus on motor tension, vigilance and scanning symptoms as the core associated symptoms of GAD (Brown, Marten, & Barlow, 1995; Marten et al., 1993; Starcevic & Bogojevic, 1999; Starcevic, Fallon, & Uhlenhuth, 1994; Tracey, Chorpita, Douban, & Barlow, 1997), far less attention has been paid to the threshold of three symptoms, despite questions about the optimal number of required symptoms (Brown et al., 1995) and the unknown impact of different thresholds on the prevalence and correlates of GAD.

These debates suggest that the GAD duration, excessiveness, and associated symptoms criteria may need to be revisited in the forthcoming revisions of DSM and ICD. However, before serious consideration is given to modifying these criteria, it is important to consider how such changes would influence the prevalence of GAD, and what implications these revisions would have for the relationship of GAD to other disorders (Maser, 1998). The finding that GAD often precedes and is a predictor of negative outcomes in disorders such as depression (e.g., Kessler et al., 1996; Schoevers, Deeg, van Tilburg, & Beekman, 2005) has underscored the clinical importance of its early diagnosis and treatment. It is critical that any proposed changes in criteria for GAD continue to have predictive validity.

Our group recently began examining the implications of modifying the GAD duration (Kessler et al., 2005b) and excessiveness (Ruscio et al., 2005) criteria using data from the US National Comorbidity Survey Replication (NCS-R) (Kessler & Merikangas, 2004). Early results indicated that relaxing either of these criteria may bring into the GAD diagnosis a sizable number of individuals with a somewhat less severe, yet still clinically significant, GAD-like syndrome. These results, although suggestive, have left several issues unresolved. First, prior research

studied the associations of modified GAD with other variables cross-sectionally. To evaluate the implications of diagnostic changes for predictive validity, there is a need for research that takes a longitudinal perspective and that controls for other major features of GAD (uncontrollability, distress, impairment) that bear on its severity and may moderate its association with other disorders. Second, prior research focused on the duration and excessiveness criteria of GAD. There is a need to extend this research to other contentious GAD criteria that are likely to be re-examined in DSM-V. A logical extension is the GAD associated symptoms criterion, which was substantially revised in DSM-IV and remains a major source of discrepancy between the DSM and ICD definitions of the disorder. Given the key role of associated symptoms in informing clinicians' pattern recognition and subsequent diagnostic judgments, it is crucial that we understand the implications of this criterion – and potential further refinements of this criterion – for the prevalence and predictive validity of GAD. Third, prior research studied the impact of altering each GAD criterion individually. As changes to diagnostic criteria are unlikely to be considered in isolation of one another, there is a need to evaluate the joint impact of modifying these criteria on the composition and utility of the GAD diagnosis.

Although modifications may have the effect of either broadening or restricting a diagnostic definition, we consider only broadened GAD definitions here. A focus on broadened definitions is justified by observed similarities between DSM-IV and subthreshold GAD on such clinically important measures as disability and treatment seeking (Kessler et al., 2005b; Ruscio et al., 2005), suggesting that the current GAD definition may be missing clinically significant cases. A broadened definition may have the added advantage of allowing more patients to receive a definitive (rather than an NOS) diagnosis, allowing better identification and treatment of GAD—especially in non-specialty, primary care settings where many anxiety cases are seen. Finally, to the extent that GAD predicts the onset of other disorders, a broadened definition has the potential to identify a higher proportion of those who develop subsequent psychopathology. If the definition could be broadened without sacrificing predictive validity, the utility of the GAD diagnosis would be increased.

The current paper uses data from the NCS-R to evaluate the implications of a broadened GAD diagnosis for estimates of prevalence and predictive validity. Increasingly broader definitions of GAD were constructed to examine the individual and joint effects of relaxing the duration, excessiveness, and associated symptoms requirements of DSM-IV. Aside from examining changes in prevalence, the main analytic focus is on the extent to which broadly defined GAD missing one or more of the above criteria predicts the subsequent first onset of temporally secondary DSM-IV disorders. This focus on prediction of secondary conditions was based partly on the assumption that a central way of defining clinical significance of subthreshold GAD is to determine whether it predisposes to other syndromes that are already considered clinically significant in the DSM system.

## 1. Method

### 1.1. Sample

The NCS-R is a nationally representative, face-to-face survey of US household residents carried out between February 2001 and December 2003. The survey used a multi-stage clustered area probability sampling design and had a response rate of 70.9%. Recruitment began with a letter and study fact brochure followed by an in-person visit by an interviewer who described the study aims and procedures and obtained verbal (rather than written) informed consent, consistent

with recruitment procedures of the baseline NCS (Kessler et al., 1994). Respondents received \$50 for their participation.

All 9282 respondents were administered a Part I psychiatric diagnostic interview by a professional survey interviewer. Of these, a subset of 5692 respondents (including those who met lifetime criteria for any Part I disorder, plus a probability sample of other Part I respondents) was also administered a Part II interview assessing additional disorders and correlates. The present analyses were performed on this Part II sample, which was weighted to adjust for the differential probabilities of respondent selection as a function of household size, more intense recruitment of hard-to-recruit individuals, higher selection probabilities of Part I respondents with a lifetime disorder, and residual variation between sample and population distributions on several geographic and socio-demographic variables in the 2000 US Census. Further details of the NCS-R sampling design and weighting procedures are provided elsewhere (Kessler et al., 2004).

### *1.2. Diagnostic assessment*

Diagnoses were derived from Version 3.0 of the WHO Composite International Diagnostic Interview (CIDI 3.0) (Kessler & Ustun, 2004), a fully structured lay-administered diagnostic interview. Blind clinical re-interviews of a probability subsample of NCS-R respondents (Kessler, Berglund, Demler, Jin, & Walters, 2005a) found generally good concordance between DSM-IV diagnoses of anxiety, mood, and substance use disorders (impulse-control disorders were not evaluated) yielded by the CIDI 3.0 and by the Structured Clinical Interview for DSM-IV (SCID) (First, Spitzer, Gibbon, & Williams, 2002). GAD was diagnosed following DSM-IV criteria, but varying the duration, excessiveness, and associated symptoms required for a diagnosis. Duration was relaxed from 6+ months to 1+ months, excessiveness was relaxed to include excessive or non-excessive worry, and associated symptoms were relaxed from 3+ to 2+ Criterion C symptoms. To avoid the potentially obfuscating effects of uncertain GAD hierarchical exclusion criteria on the association of GAD with other disorders, we did not observe diagnostic hierarchies when assigning GAD diagnoses. All other disorders were diagnosed using DSM-IV criteria following diagnostic hierarchy rules.

### *1.3. Other measures*

In addition to the DSM-IV GAD diagnosis, a measure of GAD severity was included in analyses. To construct the measure, a set of nested dichotomous variables representing uncontrollability, distress, and impairment associated with worry was submitted to a principal components analysis. The relative sizes of the unrotated eigenvalues for the first (5.9) and second (2.1) components, as well as consideration of simple structure, suggested a strong first principal component that can be interpreted as a general severity dimension. Consequently, these variables were submitted to a two-parameter item response theory (IRT) analysis using the BILOG software package (Scientific Software Inc., 1997), generating a continuous severity score that was trichotomized to divide the broadly defined GAD sample into roughly equal groups of mild (35%), moderate (32%), and severe (33%) cases.

Several socio-demographic measures were included as covariates. These included age at interview (18–29, 30–44, 45–59, 60+), sex, race-ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, other), education (student, 0–11 years, 12 years, 13–15 years, 16+ years), and marital status (currently married, previously married, never married).

#### 1.4. Statistical analysis

Cross-tabulations were used to estimate prevalence and comorbidity for progressively broader definitions of GAD. Discrete-time survival analysis (Efron, 1988), with person-year as the unit of analysis, was used to examine the associations between variably defined GAD and the subsequent onset of temporally secondary disorders. The temporal order of GAD and other disorders was determined from retrospective age-of-onset reports. In an initial baseline model, associations were estimated separately for active GAD (in which the GAD episode was still ongoing when the later disorder began) versus remitted GAD (in which the GAD episode ended before the later disorder began). Within active and remitted subsamples, associations were also estimated separately for mild, moderate, and severe GAD based on respondents' worst GAD episode in an effort to control for any confounding between the individual criteria under examination and overall disorder severity. Subsequent survival models focused on active GAD, estimating associations separately for DSM-IV GAD and for mutually exclusive subgroups who failed one or more GAD criteria. Survival coefficients were transformed to odds ratios (ORs) with 95% confidence intervals (CIs) for ease of interpretation. Multivariate significance was evaluated via Wald  $\chi^2$  tests based on coefficient variance-covariance matrices adjusted for design effects using the Taylor series linearization method (Wolter, 1985). Statistical significance was evaluated at the .05 level using two-tailed tests.

## 2. Results

### 2.1. Prevalence and comorbidity of broadly defined GAD

As expected, increasingly broader definitions of GAD are associated with increasing lifetime and 12-month prevalence of the disorder (Table 1). Prevalence increases by about 50–60% when the duration criterion is relaxed from 6 months to 1 month and by about 40% when the excessiveness requirement is dropped. By contrast, requiring two rather than three associated symptoms has little effect on prevalence, as very few respondents who endorsed Criterion C symptoms ( $n = 1819$ ) endorsed only two such symptoms ( $n = 140$ ; even fewer endorsed just one associated symptom,  $n = 68$ ). Relaxing both the duration and excessiveness criteria results in more than a doubling of GAD cases relative to the DSM-IV definition, to 12.8% (lifetime) and 6.2% (12-month). Relaxing all three criteria raises the prevalence of GAD further to 13.7% (lifetime) and 6.6% (12-month).

Increasingly broader definitions of GAD are associated with decreasing rates of comorbidity. Whereas 92% of those with the full DSM-IV GAD syndrome qualify for another lifetime DSM-IV disorder assessed in the survey, the proportion of comorbid cases is 89–91% among those missing one GAD criterion, 87–89% among those missing two criteria, and 86% among those missing all three criteria. In an absolute sense, though, the proportion of comorbid cases is high for all GAD definitions considered here.

### 2.2. Associations of GAD status and severity with the subsequent first onset of other disorders

Active GAD more consistently predicts new onsets of subsequent DSM-IV disorders than does remitted GAD (Table 2). The median OR (inter-quartile range [IQR] in parentheses) is 2.9 (1.9–3.8) for active GAD and 1.8 (1.0–2.6) for remitted GAD. The ORs for any mood disorder, any substance use disorder, and any disorder are significantly larger for active than remitted cases of broadly defined GAD.

Table 1  
Prevalence and comorbidity associated with increasingly broader definitions of GAD<sup>a</sup>

	Lifetime prevalence		12-month prevalence		Percent with lifetime comorbid disorder <sup>b</sup>	
	%	(S.E.)	%	(S.E.)	%	(S.E.)
DSM-IV GAD <sup>c</sup>	5.6	(0.3)	3.0	(0.2)	92.1	(1.5)
GAD duration criterion relaxed (1+ months duration)	9.1	(0.4)	4.5	(0.3)	89.3	(1.4)
GAD excessiveness criterion relaxed (excessive or non-excessive worry)	7.8	(0.4)	4.1	(0.3)	90.3	(1.2)
GAD associated symptoms criterion relaxed (2+ Criterion C symptoms)	5.9	(0.3)	3.2	(0.2)	90.7	(1.4)
Duration and excessiveness criteria relaxed (1+ months, excessive/non-excessive)	12.8	(0.6)	6.2	(0.4)	87.3	(1.1)
Duration and associated symptoms criteria relaxed (1+ months, 2+ C symptoms)	9.6	(0.4)	4.7	(0.3)	88.2	(1.3)
Excessiveness and associated symptoms criteria relaxed (excessive/non-excessive, 2+ C symptoms)	8.4	(0.4)	4.3	(0.3)	88.8	(1.3)
All 3 criteria relaxed (1+ months, excessive/non-excessive, 2+ C symptoms)	13.7	(0.6)	6.6	(0.4)	86.3	(1.1)

<sup>a</sup> Analyses were performed in the Part II sample ( $n = 5692$ ).

<sup>b</sup> Proportion of respondents meeting each definition of GAD who qualify for at least one other lifetime DSM-IV anxiety, mood, impulse-control, or substance use disorder assessed in the NCS-R.

<sup>c</sup> The prevalence estimates reported here are slightly lower than the estimates in earlier reports (Kessler et al., 2005a, 2005c) despite the fact that GAD is defined here without hierarchy compared to with hierarchy in the earlier reports. These somewhat lower prevalence estimates (compared to the lifetime prevalence estimate of 5.7% and 12-month prevalence estimate of 3.1% in the earlier reports) are due to the implementation of a stricter operationalization of the DSM-IV excessiveness requirement in Criterion A in the updated diagnostic algorithms.

GAD severity also predicts the onset of secondary disorders, with more severe GAD associated with higher risk of secondary disorders. For most disorders, ORs increase monotonically over the three severity levels: moderate GAD is associated with greater relative odds of later disorders than mild GAD in 21 of 27 comparisons, whereas severe GAD is associated with greater odds than moderate GAD in 24 of 29 comparisons and mild GAD in 30 of 30 comparisons. Nonetheless, severity of active GAD more consistently predicts the first onset of later anxiety and mood disorders ( $\chi^2_{1-2} = 0.8-13.4, p < .001-.672$ ) than later impulse-control or substance use disorders ( $\chi^2_{1-2} = 0.0-6.9, p = .031-.984$ ). Also, although the severity of remitted GAD is associated with later risk of any mood and any substance use disorder, it significantly predicts only one individual disorder: alcohol abuse with or without dependence ( $\chi^2_2 = 11.1, p = .004$ ).

### 2.3. Associations of variably defined GAD with the subsequent first onset of other disorders

To study associations of variably defined GAD with later disorders, holding constant the effects of GAD status and severity, we estimated associations only for active GAD and controlled for GAD severity in addition to socio-demographics. DSM-IV GAD predicts the subsequent first onset of most disorders assessed even when severity is controlled (median OR = 2.6, IQR = 1.5–3.6), significantly so for 9 of 15 disorders (Table 3). The ORs are substantially higher in predicting mood

Table 2

Associations<sup>a</sup> of GAD symptom severity with the onset of subsequent DSM-IV mental disorders, controlling for the distinction between active and remitted GAD<sup>b</sup>

	Active						$\chi^2_{1-2}$	Remitted						$\chi^2_{1-2}$	$\chi^2_{1-3}$
	Mild		Moderate		Severe			Mild		Moderate		Severe			
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)		OR	(95% CI)	OR	(95% CI)	OR	(95% CI)		
Any anxiety disorder <sup>c</sup>	3.6*	(2.4–5.5)	6.6*	(4.3–10.2)	6.2*	(3.9–9.8)	6.4**	0.9	(0.2–4.0)	–	–	2.4	(0.7–7.7)	1.1	5.7
Panic disorder	2.1*	(1.3–3.6)	3.5*	(1.9–6.3)	3.7*	(2.2–6.2)	2.8	–	–	2.1	(0.6–7.0)	1.7	(0.3–11.6)	0.0	2.2
Agoraphobia (w/o panic)	0.9	(0.1–7.1)	0.4	(0.1–3.7)	3.5*	(1.2–10.1)	4.2	–	–	2.5	(0.4–16.2)	–	–	–	1.6
Specific phobia	0.3	(0.0–2.5)	0.4	(0.0–2.7)	2.3*	(1.1–4.5)	6.0**	–	–	1.8	(0.2–14.1)	–	–	–	1.3
Social phobia	1.6	(0.7–3.8)	3.4*	(1.7–6.8)	5.6*	(3.2–9.9)	6.2**	–	–	–	–	–	–	–	–
Posttraumatic stress disorder	1.5	(0.7–3.2)	3.8*	(2.4–5.9)	4.6*	(2.7–8.0)	9.1**	0.9	(0.2–4.2)	0.7	(0.2–3.3)	2.3	(0.6–8.0)	1.6	6.4
Obsessive-compulsive disorder <sup>d</sup>	1.5	(0.2–12.1)	2.3	(0.4–12.0)	16.6*	(7.2–38.6)	9.0**	6.9	(0.9–50.7)	–	–	12.1*	(1.2–123.3)	0.2	1.3
Any mood disorder	3.2*	(2.5–4.2)	4.3*	(3.4–5.5)	7.7*	(5.8–10.2)	23.9**	0.5	(0.2–1.4)	1.9*	(1.0–3.8)	2.9*	(1.3–6.5)	7.4**	32.1***
Major depressive disorder	3.0*	(2.2–4.1)	3.4*	(2.5–4.6)	3.6*	(2.9–4.5)	0.8	0.5	(0.1–1.5)	1.0	(0.4–2.7)	1.8	(0.8–4.3)	3.2	16.7***
Dysthymic disorder	3.3*	(1.1–9.9)	3.3*	(1.5–7.3)	6.2*	(3.5–11.0)	1.8	–	–	–	–	1.2	(0.1–9.3)	–	2.4
Bipolar (I, II or sub-threshold)	2.0	(0.9–4.8)	4.8*	(2.8–8.0)	8.7*	(4.9–15.3)	13.4**	0.5	(0.1–3.6)	3.6*	(1.6–8.1)	2.5	(0.7–8.9)	4.7	9.4***
Any impulse-control disorder <sup>e</sup>	1.4	(0.5–4.1)	3.0*	(1.5–6.0)	4.4*	(2.4–7.9)	3.3	1.6	(0.2–13.8)	–	–	2.8	(0.3–28.6)	0.1	0.2
Oppositional-defiant disorder <sup>e</sup>	0.4	(0.0–2.8)	2.5	(0.7–9.5)	4.1*	(1.9–8.8)	6.9**	–	–	–	–	–	–	–	–
Conduct disorder <sup>e</sup>	0.6	(0.1–4.4)	2.2	(0.7–7.3)	3.8*	(1.7–8.6)	3.4	–	–	–	–	–	–	–	–
Attention-deficit/hyperactivity <sup>e</sup>	–	–	4.6	(0.8–28.1)	0.9	(0.3–3.0)	2.4	–	–	–	–	–	–	–	–
Intermittent explosive disorder	2.4*	(1.0–5.9)	3.9*	(2.0–7.5)	4.9*	(2.8–8.6)	1.7	1.4	(0.2–11.3)	2.6	(0.4–18.8)	4.7*	(1.0–22.4)	1.0	0.4
Any substance use disorder	1.7*	(1.0–2.8)	2.4*	(1.6–3.7)	2.5*	(1.6–3.9)	2.3	0.5	(0.1–2.3)	0.2	(0.0–1.7)	2.9*	(1.4–6.1)	9.1**	7.9***
Alcohol abuse w/or w/o dependence	1.7*	(1.1–2.6)	3.0*	(2.0–4.3)	2.5*	(1.6–4.0)	5.0	0.5	(0.1–2.4)	0.2	(0.0–1.7)	3.5*	(1.8–6.6)	11.1**	9.2***
Drug abuse w/or w/o dependence	2.7*	(1.6–4.6)	2.7*	(1.7–4.4)	2.9*	(1.5–5.5)	0.0	–	–	–	–	2.0	(0.4–9.9)	–	0.2
Any disorder <sup>c</sup>	4.8*	(3.5–6.5)	8.9*	(4.8–16.6)	11.0*	(7.1–17.0)	12.6**	0.9	(0.3–2.6)	1.3	(0.3–4.7)	6.7*	(2.0–22.8)	7.4**	23.3***

<sup>a</sup> Results are based on a discrete-time survival model with person-year as the unit of analysis. The model controlled for person-year, age at interview, sex, race-ethnicity, education level, and marital status. Associations are expressed as a function of GAD symptom severity, with ORs for no GAD set to 1.0. Endashed lines indicate that an OR could not be estimated due to insufficient *n*. Degrees of freedom for  $\chi^2$  tests were determined by the number of groups available for each comparison.

<sup>b</sup> Disorders were defined using DSM-IV criteria including organic exclusion rules; diagnostic hierarchy rules were observed for all disorders other than GAD. GAD was broadly defined to include respondents whose worst GAD episode lasted at least 1 month, involved excessive or non-excessive worry, and included two or more associated symptoms from Criterion C. The sample included respondents with no lifetime GAD (*n* = 4414) plus respondents with a history of mild (*n* = 433), moderate (*n* = 418), or severe (*n* = 427) GAD. Active cases were those whose GAD episode began before the onset year of the subsequent disorder and was ongoing when this disorder began. Remitted cases were those whose GAD episode ended prior to the onset of the subsequent disorder.

<sup>c</sup> No adjustment was made for the fact that one or more disorders in the category were not assessed for all Part II respondents.

<sup>d</sup> Assessed in a random one-third of the Part II sample (*n* = 2073).

<sup>e</sup> Analyses restricted to Part II respondents in the age range 18–44 years (*n* = 3197).

\* OR significant at the .05 level, 2-sided test.

\*\* Significant difference between ORs for different GAD severity levels at the .05 level.

\*\*\* Significant difference between ORs for active and remitted GAD cases at the .05 level.

**Table 3**  
 Associations<sup>a</sup> of variably defined GAD with the onset of subsequent DSM-IV mental disorders,<sup>b</sup> controlling for GAD severity

	DSM-IV GAD		Mutually exclusive subgroups of broadly defined GAD											
	OR	(95% CI)	Failed duration criterion only			Failed excessiveness criterion only			Failed associated symptoms criterion only			Failed two or more of the three criteria		
			OR	(95% CI)	$\chi^2_1$	OR	(95% CI)	$\chi^2_1$	OR	(95% CI)	$\chi^2_1$	OR	(95% CI)	$\chi^2_1$
Any anxiety disorder <sup>c</sup>	2.6*	(1.3–5.1)	3.4*	(1.8–6.6)	0.4	2.5	(1.0–6.3)	0.0	1.7	(0.3–12.0)	0.2	2.1	(0.9–5.2)	0.2
Panic disorder	3.8*	(2.0–7.0)	3.0*	(1.3–7.2)	0.2	0.9	(0.2–3.4)	5.3**	–	–	–	1.8	(0.6–5.5)	1.7
Agoraphobia (w/o panic)	1.5	(0.2–11.5)	0.9	(0.0–39.6)	0.2	0.7	(0.1–7.7)	0.5	5.6	(0.5–58.8)	1.1	–	–	–
Specific phobia	0.6	(0.1–4.5)	0.6	(0.0–7.6)	0.0	0.2	(0.0–12.5)	0.9	–	–	–	–	–	–
Social phobia	2.6	(1.0–6.9)	3.6*	(1.4–9.5)	0.5	1.2	(0.3–4.4)	1.9	1.5	(0.1–22.3)	0.2	0.6	(0.1–4.3)	1.5
Posttraumatic stress disorder	2.2*	(1.0–4.8)	1.5	(0.6–3.8)	0.7	1.4	(0.4–4.7)	0.8	0.7	(0.1–6.9)	1.3	1.7	(0.6–4.8)	0.3
Obsessive-compulsive disorder <sup>d</sup>	1.6	(0.2–13.7)	3.9	(0.3–45.8)	1.2	–	–	–	–	–	–	–	–	–
Any mood disorder	4.8*	(3.5–6.6)	3.0*	(1.9–4.7)	5.0**	3.8*	(2.3–6.2)	1.0	1.2	(0.3–4.9)	3.8	2.7*	(1.4–5.2)	2.6
Major depressive disorder	3.4*	(2.4–4.8)	3.2*	(1.9–5.5)	0.0	3.5*	(2.0–6.3)	0.0	2.5	(0.9–7.1)	0.3	3.0*	(1.6–5.6)	0.2
Dysthymic disorder	4.0*	(1.2–13.3)	1.4	(0.3–6.6)	1.5	11.1*	(2.8–44.0)	6.1**	5.1	(0.5–47.7)	0.0	1.5	(0.2–11.8)	0.7
Bipolar (I, II or sub-threshold)	4.2*	(1.9–9.6)	1.9	(0.6–6.0)	5.2**	1.3	(0.4–4.6)	6.4**	–	–	–	1.3	(0.4–4.5)	5.9**
Any impulse-control disorder <sup>e</sup>	1.6	(0.5–5.1)	1.9	(0.5–6.7)	0.1	0.1	(0.0–1.2)	5.8**	–	–	–	2.6	(0.6–11.3)	0.8
Oppositional-defiant disorder <sup>e</sup>	0.7	(0.1–7.5)	0.6	(0.1–5.0)	0.0	0.2	(0.0–3.7)	1.3	–	–	–	–	–	–
Conduct disorder <sup>e</sup>	0.8	(0.2–3.9)	0.5	(0.1–2.9)	0.5	0.1*	(0.0–0.3)	4.2**	–	–	–	1.1	(0.1–20.7)	0.1
Attention-deficit/hyperactivity <sup>e</sup>	7.3*	(1.2–44.9)	0.0*	(0.0–0.0)	132.4**	4.7	(0.3–62.4)	0.1	–	–	–	–	–	–
Intermittent explosive disorder	3.5*	(1.3–9.2)	1.7	(0.5–6.0)	1.8	1.7	(0.4–7.6)	1.0	1.1	(0.1–10.4)	1.1	3.8*	(1.1–13.0)	0.0
Any substance use disorder	1.8*	(1.1–3.1)	2.0*	(1.2–3.5)	0.2	1.6	(0.8–3.4)	0.1	1.3	(0.4–4.6)	0.3	2.2*	(1.1–4.4)	0.2
Alcohol abuse w/or w/o dependence	1.7*	(1.0–2.8)	2.3*	(1.3–4.1)	1.9	1.7	(0.8–3.3)	0.0	1.0	(0.2–4.8)	0.4	2.1*	(1.1–4.0)	0.4
Drug abuse w/or w/o dependence	3.5*	(1.9–6.5)	2.7*	(1.4–5.3)	0.5	1.5	(0.4–5.5)	2.0	1.4	(0.3–7.2)	1.6	4.6*	(2.2–9.4)	0.5
Any disorder <sup>c</sup>	1.9	(1.0–3.6)	2.7*	(1.7–4.4)	1.1	2.7*	(1.3–5.6)	1.5	0.6	(0.1–4.0)	2.0	1.2	(0.4–3.6)	0.7

<sup>a</sup> Results are based on a discrete-time survival model with person-year as the unit of analysis. The model controlled for person-year, age at interview, sex, race-ethnicity, education level, marital status, and GAD severity. Associations are expressed as a function of GAD definition, with ORs for no GAD set to 1.0. Endashed lines indicate that an OR could not be estimated due to insufficient *n*.

<sup>b</sup> Disorders were defined using DSM-IV criteria including organic exclusion rules; diagnostic hierarchy rules were observed for all disorders other than GAD. GAD was broadly defined to include respondents whose worst GAD episode lasted at least 1 month, involved excessive or non-excessive worry, and included two or more associated symptoms from Criterion C. Respondents with active, broadly defined GAD were sorted into five mutually exclusive subgroups based on the most stringent definition of GAD that they met. The sample included respondents with no lifetime GAD (*n* = 4414) plus respondents with DSM-IV GAD (*n* = 538), GAD failing duration only (*n* = 298), GAD failing excessiveness only (*n* = 208), GAD failing associated symptoms only (*n* = 35), and GAD failing two or more of these three criteria (*n* = 199).

<sup>c</sup> No adjustment was made for the fact that one or more disorders in the category were not assessed for all Part II respondents.

<sup>d</sup> Assessed in a random one-third of the Part II sample (*n* = 2073).

<sup>e</sup> Analyses restricted to Part II respondents in the age range 18–44 years (*n* = 3197).

\* OR significant at the .05 level, 2-sided test.

\*\* Significant difference between ORs for DSM-IV GAD and broadly defined GAD subgroups at the .05 level.



Table 4

Associations<sup>a</sup> of variably defined GAD with the onset of subsequent DSM-IV mental disorders<sup>b</sup> among respondents whose GAD preceded the subsequent disorder by at least 5 years<sup>c</sup>

	DSM-IV GAD		Mutually exclusive subgroups of broadly defined GAD											
	OR	(95% CI)	Failed duration criterion only			Failed excessiveness criterion only			Failed associated symptoms criterion only			Failed two or more of the three criteria		
			OR	(95% CI)	$\chi^2_1$	OR	(95% CI)	$\chi^2_1$	OR	(95% CI)	$\chi^2_1$	OR	(95% CI)	$\chi^2_1$
Any anxiety disorder <sup>d</sup>	3.3*	(2.0–5.5)	4.5*	(1.6–12.0)	0.3	2.7	(1.0–7.4)	0.1	1.7	(0.1–20.8)	0.3	2.9*	(1.0–8.6)	0.0
Any mood disorder	6.2*	(5.0–7.8)	2.8*	(1.5–5.1)	6.0**	5.3*	(3.1–8.9)	0.3	0.9	(0.1–10.3)	2.6	2.4*	(1.2–4.8)	6.8**
Any impulse-control disorder <sup>c</sup>	1.6	(0.4–6.1)	1.4	(0.2–12.4)	0.0	–	–	–	–	–	–	5.8	(0.9–36.3)	1.3
Any substance use disorder	2.2*	(1.4–3.5)	2.6*	(1.5–4.5)	0.2	1.6	(0.5–4.8)	0.4	3.1	(0.9–11.1)	0.3	2.2*	(1.0–5.0)	0.0
Any disorder <sup>d</sup>	2.5*	(1.6–3.9)	4.8*	(1.9–12.1)	1.5	5.3*	(2.6–10.9)	3.3	1.0	(0.1–14.4)	0.5	1.2	(0.4–3.6)	1.6

<sup>a</sup> Results are based on a discrete-time survival model with person-year as the unit of analysis. The model controlled for person-year, age at interview, sex, race-ethnicity, education level, and marital status. GAD severity was not controlled. Associations are expressed as a function of GAD definition, with ORs for no GAD set to 1.0. Endashed lines indicate that an OR could not be estimated due to insufficient *n*.

<sup>b</sup> Due to sparse data, secondary disorders were combined into the broad categories of any anxiety disorder (panic disorder, agoraphobia, specific phobia, social phobia, posttraumatic stress disorder, or obsessive-compulsive disorder), any mood disorder (major depressive disorder, dysthymic disorder, or bipolar spectrum), any impulse-control disorder (oppositional-defiant disorder, conduct disorder, attention-deficit/hyperactivity disorder, or intermittent explosive disorder), any substance use disorder (alcohol abuse or dependence or drug abuse or dependence), and any of the above disorders. Disorders were defined using DSM-IV criteria including organic exclusion rules; diagnostic hierarchy rules were observed for all disorders other than GAD.

<sup>c</sup> GAD was broadly defined to include respondents whose worst GAD episode lasted at least 1 month, involved excessive or non-excessive worry, and included two or more associated symptoms from Criterion C. Respondents with active, broadly defined GAD were sorted into five mutually exclusive subgroups based on the most stringent definition of GAD that they met. The sample included respondents with no lifetime GAD (*n* = 4414) plus respondents with DSM-IV GAD (*n* = 538), GAD failing duration only (*n* = 298), GAD failing excessiveness only (*n* = 208), GAD failing associated symptoms only (*n* = 35), and GAD failing two or more of these three criteria (*n* = 199). Results presented are for the subsample of respondents whose onset of GAD preceded the onset of the secondary disorder by at least 5 years and was still ongoing when this disorder began.

<sup>d</sup> No adjustment was made for the fact that one or more disorders in the category were not assessed for all Part II respondents.

<sup>e</sup> Analyses restricted to Part II respondents in the age range 18–44 years (*n* = 3197).

\* OR significant at the .05 level, 2-sided test.

\*\* Significant difference between ORs for DSM-IV GAD and broadly defined GAD subgroups at the .05 level.

(OR = 4.8) and anxiety (OR = 2.6) disorders than substance-use (OR = 1.8) and impulse-control (OR = 1.6) disorders.

Overall, the full GAD syndrome is associated with a higher risk of subsequent disorders than is GAD in which one or more criteria are not met. The odds of new disorder onsets are highest for DSM-IV GAD, lower for GAD lasting less than six months (median OR = 1.7, IQR = 0.8–2.9), and lower still for GAD involving only two associated symptoms (median OR = 1.5, IQR = 1.1–3.2) or non-excessive worry (median OR = 1.4, IQR = 0.7–1.7). Few of the differences in ORs between DSM-IV GAD and the subthreshold GAD subgroups are statistically significant. Nevertheless, declining ORs outnumber increasing ORs by at least 3:1 across all disorders. Moreover, differences that are significant almost uniformly reveal lower odds of later disorders for partial than full GAD, with the most consistently diminished risk found for the bipolar spectrum ( $\chi^2_1 = 5.2$ – $6.4$ ,  $p = .011$ – $.023$ ). The sole exception is a substantially elevated risk of subsequent dysthymic disorder among respondents with non-excessive worry (OR = 11.1,  $\chi^2_1 = 6.1$ ,  $p = .014$ ).

#### 2.4. Sensitivity analyses

Sensitivity analyses were performed without controlling for GAD severity to see whether further significant differences would emerge between full and partial GAD (results not shown, but available on request). There was an across-the-board increase in the strength of associations between GAD and later disorders, both for the full DSM-IV syndrome (median OR = 4.0, IQR = 3.5–5.4) and for subgroups failing one or more of the three criteria (median OR = 2.7, IQR = 1.5–3.3). The overall pattern of results, though, was the same, with consistently smaller ORs associated with partial than full GAD and the same few disorders yielding significant results.

To evaluate the robustness of these results, analyses were replicated within the more conservative subsample of respondents whose GAD episode preceded the onset of the secondary disorder by a minimum of 5 years. To enhance statistical power, we performed analyses using five broad categories of secondary disorders (anxiety, mood, impulse-control, substance-use, and any disorder). Consistent with earlier category-level results, DSM-IV GAD is a particularly strong predictor of first onsets of later mood disorders (OR = 6.2), a somewhat weaker predictor of later anxiety disorders (OR = 3.3), and a considerably weaker predictor of later substance-use (OR = 2.2) and impulse-control (OR = 1.6) disorders (Table 4). The association with secondary mood disorders is weaker for three of the subthreshold GAD subgroups (OR = 0.9–2.8) than for the full GAD syndrome (OR = 6.2;  $\chi^2_1 = 2.6$ – $6.8$ ,  $p = .009$ – $.109$ ), an effect that earlier was shown to be due mainly to diminished risk for bipolar spectrum conditions. The exception is GAD without excessive worry (OR = 5.3,  $\chi^2_1 = 0.3$ ,  $p = .575$ ), which was found in earlier analyses to be due to elevated odds of dysthymic disorder offsetting the diminished odds of bipolar spectrum in this subgroup.

### 3. Discussion

The present findings must be interpreted in light of two important study limitations. First, all disorders included in these analyses were assessed by fully structured interviews administered by professional lay interviewers. Such interviews often generate more reliable diagnoses than semi-structured clinical interviews (Wittchen, 1994), and their prevalence estimates typically correspond well to diagnoses yielded by semi-structured clinical interviews (Kessler et al., 2005a). Nevertheless, fully structured assessments limit the sorts of symptom clarification and cross-disorder questions that facilitate differential diagnosis, and this may have led to inflated

associations between GAD and other disorders. Second, the temporal order of disorders was determined from retrospective age-of-onset reports. While we used a probing strategy that has been shown to improve recall of age of onset (Knauper, Cannell, Schwarz, Bruce, & Kessler, 1999), there were doubtlessly residual errors, perhaps especially when distinguishing GAD from disorders with overlapping symptoms. To help mitigate this concern, we performed sensitivity analyses within subsamples reporting an onset of GAD at least 5 years before the comorbid disorder. Prospective longitudinal research would be needed to more definitively establish the temporal priority and prospective associations of GAD with other disorders.

Within the context of these limitations, we found that broadening the GAD diagnosis in the three ways considered here would more than double the prevalence of the disorder. Most of the increase in prevalence comes from reducing the minimum duration to 1 month and, to a lesser extent, from eliminating the excessive worry requirement. Prevalence is minimally affected by requiring two rather than three associated symptoms. As the GAD definition is broadened, there is a slight but consistent decrement in the comorbidity of GAD with other disorders. This small decrement is apparent both in cross-sectional analyses of lifetime comorbidity and in longitudinal analyses estimating the odds of subsequent disorder onsets. However, few of the differences are sufficiently large to reach statistical significance. The overall pattern of results is the same regardless of whether GAD severity is controlled and even when the onsets of GAD and later disorders are separated by at least 5 years.

These results join a growing dialogue about the optimal definition of GAD and the implications of revising some of its more controversial criteria in DSM-V and ICD-11. Our finding that relaxing these criteria leads to a sizable influx of new GAD cases inevitably raises questions about how high a rate of GAD is plausible and whether new cases are sufficiently severe to merit a diagnosis. It is clear that a broadened definition would lead to more widespread diagnosis than the GAD definitions in DSM-III, III-R, and IV, which have an estimated lifetime prevalence of 4–7% in the US population (Blazer, Hughes, George, Swartz, & Boyer, 1991; Grant et al., 2005; Kessler et al., 2005a; Wittchen, Zhao, Kessler, & Eaton, 1994). Perhaps the more critical issue, though, is whether broadly defined GAD is likely to be more valid and clinically useful than DSM-IV GAD. Theorists disagree about the optimal diagnostic criteria for distinguishing normal from pathological general anxiety (Barlow & Wincze, 1998; Rickels & Rynn, 2001) and even about whether GAD is best conceived as a clinical syndrome, an anxious temperament type, or some combination of the two (Akiskal, 1998; Rickels & Schweizer, 1995). Such disagreement is particularly pronounced in debates over the DSM-IV excessiveness criterion, which has been criticized for focusing on characterological anxiety and excluding people whose anxiety is associated with severe or chronic stress (Kessler & Wittchen, 2002). As in the case of depression, it is possible that distinguishing between endogenous and reactive anxiety is not useful for optimal diagnosis and treatment, and that a broader GAD construct would have greater clinical utility than the current narrowly defined syndrome. This is supported by indications that some cases falling below the GAD threshold are sufficiently similar to diagnosed cases that their inclusion may improve the validity of the diagnosis. Important similarities have previously been observed in functional impairment, socio-demographic features, family history of GAD, and other key correlates between the full GAD syndrome and GAD lasting as little as 1 month (Bienvenu, Nestadt, & Eaton, 1998; Carter, Wittchen, Pfister, & Kessler, 2001; Hunt, Issakidis, & Andrews, 2002; Kendler et al., 1992; Kessler et al., 2005b; Maier et al., 2000; Wittchen et al., 2002) or involving non-excessive worry (Bienvenu et al., 1998; Ruscio et al., 2005).

Consistent with these results, we found few significant differences in the associations of GAD with later disorders as a function of GAD duration or excessiveness. This finding casts further

doubt on the DSM-IV 6-month duration and excessive-worry requirements, which appear to miss individuals who not only suffer from significant generalized anxiety, but have an elevated risk of developing additional disorders. While our results suggest similar conclusions about the requirement of three associated symptoms, it remains to be seen whether requiring fewer symptoms results in a clinically significant syndrome that is distinguishable from normal anxiety and transient stress reactions (Breslau & Davis, 1985; Spitzer & Williams, 1984). An alternate possibility is that requiring *more* associated symptoms would result in a more valid GAD diagnosis that more powerfully predicts important outcomes. It is noteworthy in this regard that, in a clinical sample, Brown et al. (1995) found a threshold of four rather than three associated symptoms to maximize diagnostic sensitivity (i.e., correspondence with DSM-III-R GAD diagnoses) and specificity (i.e., distinction from other anxiety and mood disorders). Thus, there is a need for systematic study of all possible thresholds along the associated symptoms criterion in relation to a wide range of correlates in both clinical and community samples. Finally, and crucial for the issue of predictive validity, we found that individuals missing two or more GAD criteria did not differ significantly from diagnosed cases in their risk for most subsequent disorders. There is a need to examine the severity and disability experienced by such individuals, who in our sample comprised more than one-quarter of new cases of broadly defined GAD. There is also a need to determine whether early diagnosis and treatment of broadly defined GAD would be effective in decreasing symptoms, improving associated disability, and preventing the subsequent development of comorbid disorders.

The present results run counter to concerns that less restrictive diagnostic criteria may lead to poorer differentiation of GAD from other disorders. If anything, we found the opposite effect: a slight reduction in associations with most other disorders as these GAD criteria are relaxed, with the most consistent reduction observed for later bipolar spectrum conditions. One possible explanation is that broadening the definition of GAD brings less severe cases into the diagnosis, and that lower rates of psychiatric comorbidity among less severe cases (Andrews, Slade, & Issakidis, 2002; Kessler, Chiu, Demler, Merikangas, & Walters, 2005c) diminish the comorbidity associated with GAD. This explanation is partly supported by the association of GAD severity with risk of later disorders, especially mood and anxiety disorders, in our sample. In contrast to this general pattern, we found the odds of subsequent dysthymic disorder to be substantially higher for non-excessive than excessive GAD. Previous studies have documented very strong associations between GAD and dysthymia in both community (Andrews et al., 2002) and clinical (Pini et al., 1997) samples, suggesting that dysthymia may be a particularly challenging boundary condition for GAD and that broadening the GAD diagnosis to include non-excessive worriers may further impede differentiation of these conditions. Alternatively, the higher odds may reflect a genuine increase in the co-occurrence of these two disorders. It is possible, for example, that an individual exposed to a chronic, objectively severe stressor may at first experience a proportionate (non-excessive) anxiety response and, over time, develop persistent feelings of hopelessness and dysphoria. Future research will need to distinguish these possibilities, and to consider further refinements to the GAD definition that facilitate its distinction from neighboring conditions and improve its detection and appropriate treatment.

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