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## Anxious distress in depressed outpatients: Prevalence, comorbidity, and incremental validity

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### Abstract

The goals of this study were to estimate the prevalence of the *DSM-5* anxious distress specifier (AD) among depressed outpatients, to examine associations of AD with comorbid diagnoses, and to test the incremental validity of AD over comorbidity in predicting functional impairment and severity of anxiety and depression symptoms. The sample was 237 outpatients diagnosed with major depressive disorder (MDD) or persistent depressive disorder (PDD), with and without AD, using the Anxiety and Related Disorders Interview Schedule for *DSM-5*. Outpatients also completed self-report questionnaires assessing functional impairment and anxiety, stress, and depression symptom severity. Two-by-two contingency tables were used to examine the associations of AD with comorbidity. Two-thirds (66.2%) of outpatients were assigned AD, with similar rates among those with MDD and PDD. Outpatients with AD were significantly more likely than those without AD to have a comorbid GAD diagnosis (OR = 2.47). Hierarchical multiple regressions were used to test the incremental validity of AD in predicting functional impairment and symptom outcomes beyond comorbid disorders. Controlling for comorbid disorders, AD was significantly associated with more severe functional impairment, autonomic arousal, stress, panic, generalized anxiety, and depression. The strongest incremental association were observed between AD and autonomic arousal ( $f^2 = 0.12-0.18$ ) and generalized anxiety ( $f^2 = 0.17$ ). These findings add to a growing literature that AD is common among outpatients and associated with important clinical outcomes, suggesting that AD should be routinely assessed in patients with mood disorders.

### Keywords

Anxious distress; *DSM-5*; Major depression; Persistent depression; Comorbidity

## 1. Introduction

The *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* (American Psychiatric Association, 2013) now includes an anxious distress specifier (AD) for mood disorders

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operationalized by five symptoms of anxiety: feeling keyed up or tense, restlessness, difficulty concentrating due to worry, feeling that something awful may happen, and feeling that one may lose control of oneself. To assign the specifier, at least two of the symptoms must occur the “majority” of days with the mood disorder. The inclusion of the AD specifier was based on evidence that individuals who experience elevated anxiety during depressive episodes have a more chronic clinical course and poorer treatment outcomes than depressed individuals without significant anxiety (Coryell et al., 1992; Fava et al., 2008, 2004). The AD specifier was added to *DSM-5* to provide diagnosticians with a simple method of labeling anxiety symptoms occurring during the course of a mood disorder (Ionescu et al., 2013).

Data were not available to evaluate the validity of the AD specifier prior to release of *DSM-5*. Preliminary research nonetheless suggests that AD is highly prevalent, occurring in 50–75% of individuals with major depressive disorder (MDD) (Hasin et al., 2018; McIntyre et al., 2016; Zimmerman et al., 2014), and that AD may outperform comorbid anxiety diagnoses in predicting important clinical correlates such as disability, depression chronicity, and treatment outcome (Gaspersz et al., 2017a, 2017b). However, the extant literature has been limited by the fact that cases of AD were identified using assessment methods that indirectly assess AD symptoms as defined in *DSM-5*. Studies collecting data prior to *DSM-5* assessed AD criteria using items from questionnaires developed for other purposes (i.e., using proxy symptoms worded differently than *DSM-5*) (Gaspersz et al., 2017a, 2017b; McIntyre et al., 2016), while the only questionnaire of *DSM-5* AD assesses symptoms over the past week rather than over the majority of days with depression (thus omitting a diagnostic requirement) (Zimmerman et al., 2014). Likewise, a recent epidemiological study of *DSM-5* MDD found AD to be highly prevalent and associated with MDD severity and poor functioning (Hasin et al., 2018), but operationalized AD based on symptoms being present for “at least two weeks” during the period when depression/anhedonia was the worst (i.e., less conservative than the *DSM-5* “majority of days” requirement).

Although an AD clinical interview was recently developed and confirmed a high rate of AD among patients with MDD in a partial hospital program (Zimmerman et al., 2017), rates among outpatients with MDD have yet to be examined. The prevalence of AD within the context of persistent depressive disorder (PDD), a new diagnosis in *DSM-5*, has also not been established. Given the strict requirement of having PDD symptoms for at least two years, it is possible that individuals with PDD are less likely to experience AD symptoms “the majority of days” (i.e., over many years) than individuals with MDD (who have been depressed for a few weeks or months). In addition, studies have not evaluated the incremental validity of clinician-assessed AD over *DSM-5* anxiety disorder diagnoses. This was recently suggested as an important direction for future research (Zimmerman et al., 2017) as AD may not offer incremental validity over comorbid disorders characterized by similar symptoms (i.e., tension, restlessness, and worry are characteristic of GAD; fear of losing control characteristic of panic attacks).

Accordingly, the current study aims were: (a) to use a semi-structured clinical interview to assess AD and estimate its prevalence among outpatients with MDD and PDD, (b) to examine the associations of AD with comorbid internalizing disorders characterized by

similar symptoms, and (c) to test the incremental validity of AD over *DSM-5* diagnoses in predicting dimensional clinical correlates. It was hypothesized that over 50% of outpatients would have AD, and that AD would be positively associated with comorbid generalized anxiety disorder (GAD) and panic disorder (PD) due to symptom overlap with AD. Given preliminary evidence that AD is significantly associated with symptom severity and impairment when controlling for the presence of comorbid anxiety disorders (Gaspersz et al., 2017a, 2017b), it was also hypothesized that AD would predict unique variance in a wide range of the dimensional clinical correlates (e.g., severity of functional impairment, anxiety and depression symptoms) above and beyond comorbid diagnoses.

## 2. Material and methods

### 2.1. Sample

The sample consisted of 237 adults with a current *DSM-5* unipolar depressive disorder diagnosis seeking assessment and treatment at a large outpatient clinic specializing in cognitive-behavioral treatments for internalizing disorders (i.e., anxiety and related disorders). The sample was predominately Caucasian (75.5%; African-American = 8.4%; Asian = 13.1%; Other = 2.5%), mostly female (57.8%), and the average age was 31.5 ( $SD = 12.9$ , range 18–82).

**Procedures.**—The intake assessment involved completing a semi-structured interview and self-report questionnaires as part of a larger study examining the severity, course, and classification of internalizing disorders. The current sample was drawn from this larger study (i.e., the 31.6% with MDD or PDD). Inclusion and exclusion criteria for the study were first assessed by telephone screening upon initial contact for clinical services. Inclusion criteria were being at least 18 years old and reporting a complaint likely related to an internalizing disorder. Exclusionary criteria included: (a) current hallucinations or delusions, (b) severe suicide/homicide risk meriting immediate crisis intervention, and (c) two or more hospitalizations in the past five years for psychotic symptoms. Patients were also required to meet psychotropic medication and psychotherapy stabilization criteria prior to completing the assessment (anxiolytics: stable dosage for at least four weeks; antidepressants, antipsychotics, and psychotherapy: stable dosage/type for at least 6 weeks). The wash out period (i.e., period since medication discontinuation) was four weeks for antidepressants and antipsychotics and two weeks for anxiolytics. Eligible patients were invited to complete the in-person assessment, at which time inclusion and exclusion criteria were confirmed. Written informed consent was obtained prior to beginning the in-person interview. All study procedures were approved by the governing Institutional Review Board.

### 2.2. Measures

**Diagnoses.**—Current diagnoses were established using the Anxiety and Related Disorders Interview Schedule for *DSM-5* (ADIS-5-L) (Brown and Barlow, 2014), a semi-structured interview designed to obtain reliable diagnosis of *DSM-5* anxiety, mood, obsessive-compulsive, trauma/stress, and somatic symptom disorders, and to screen for the presence of other conditions (e.g., eating disorders; psychotic disorders). In most ADIS-5-L sections, diagnosticians make dimensional ratings (0–8) of disorder symptoms and associated

features. A dimensional clinical severity rating of symptom interference and distress is also assigned to *DSM-5* diagnoses (0–8), with a rating of 4 or higher reflecting a “clinical” disorder (i.e., meeting *DSM-5* criteria). The disorder associated with the highest level of distress and impairment is referred to as the *principal* diagnosis. A slightly larger proportion of the sample was diagnosed with current MDD (54.9%) than PDD (45.1%). MDD and PDD were the principal diagnosis for 17.3% and 19.0% of the total sample, respectively. Roughly one-third of PDD patients were assigned PDD with persistent MDD (28.3%) or PDD with intermittent episodes-with current MDD (30.2%), whereas one-fifth were assigned PDD with intermittent episodes-without current MDD (22.6%) or PDD with pure dysthymic syndrome (18.9%). The most common comorbid disorders were: generalized anxiety disorder (GAD; 59.5%), social anxiety disorder (52.3%), panic disorder (PD; 17.3%), agoraphobia (17.3%), obsessive-compulsive disorder (12.7%), specific phobia (11.0%), and posttraumatic stress disorder (9.3%). Although data on ADIS-5L inter-rater diagnostic reliability are forthcoming, its predecessor demonstrated good-to-excellent interrater reliability for most DSM-IV emotional disorders, including those with negligible changes in *DSM-5* (e.g., MDD, GAD, social anxiety; Brown et al., 2001). In addition, all diagnosticians underwent extensive training and met strict certification criteria in the administration of the ADIS-5-L (described below).

Diagnosticians were five clinical psychologists and five advanced clinical doctoral students. Before participating in the study, training involved two main phases that began with expanding familiarity with the assessment tool and then formally testing trainer/trainee concordance on all ratings and diagnoses. Training began with the trainees reading the ADIS-5-L administration manual, and then observing at least two live ADIS-5-L interviews conducted by a senior, certified interviewer. While observing live interviews, the trainee made all ratings and diagnoses alongside the senior interviewer. After the interview, the trainee and senior interviewer compared and discussed diagnoses and dimensional ratings. After observing at least two live interviews, trainees would conduct two collaborative assessments using the ADIS-5-L. In a collaborative interview, the trainee assumed primary responsibility for ADIS-5-L administration, and the senior interviewer could interject as needed (e.g., ask differential diagnosis questions the trainee had not asked or provide an indication of when to skip a diagnostic section). Once trainees completed two observed and two collaborative interviews, they entered the formal “matching” process to determine training certification.

Once the trainee entered the formal certification process, they needed to meet strict criteria for their training to be considered complete. Within three of five consecutive interviews, the trainee’s diagnoses had to match the senior interviewers’ diagnoses, and the trainee had to commit no ADIS-5-L administration errors (e.g., omission of mandatory inquiries, failure to ask necessary follow-up questions for diagnostic clarification). A diagnostic match was defined as agreement of the trainee with the senior interviewer on current principal and all additional diagnoses, including *DSM-5* specifiers, within one point on the clinical severity rating for all disorders rated 4 or higher. Agreement on the clinical severity ratings of diagnoses not formally assessed in the ADIS-5-L (e.g., eating disorders) was not required.

**Anxious distress.**—The MDD and PDD sections of the ADIS-5-L include questions which assess AD symptoms occurring within the context of depressive episodes. For each of the five symptoms, diagnosticians make a severity rating between 0 (none) and 8 (very severe) and indicate whether (yes-no) the symptom has been present the majority of the days of the depressive episode. Following *DSM-5* guidelines, diagnosticians assigned the specifier when two or more AD symptoms were determined to be clinically significant and present for the majority of days in the depressive episode.

**Functional impairment.**—Overall interference and distress due to mental disorder symptoms was rated by diagnosticians using a 0 (none) to 8 (very severely disturbing/disability) scale. The Work and Social Adjustment Scale (WSAS) (Hafner and Marks, 1976), a self-report scale of functional impairment due to symptoms, was used to assess interference within five domains (work, home management, private leisure, social leisure, family). The dependent variable representing overall self-reported functional impairment was created by summing scores across domains. The reliability and validity of the WSAS has been well supported in clinical samples (Mataix-Cols et al., 2005; Mundt et al., 2002).

**Dimensions of symptom severity.**—Several dimensional measures of internalizing disorder symptoms were also collected at intake. We examined multiple measures of the clinical constructs of interest when available (e.g., depression and autonomic arousal) to determine the stability/replicability of associations with AD. Depression severity was assessed using the Beck Depression Inventory-II (Beck et al., 1996) and depression subscale of the Depression Anxiety and Stress Scales-21 (DASS) (Lovibond and Lovibond, 1995). Severity of autonomic arousal (i.e., anxiety symptoms) was assessed using the Beck Anxiety Inventory (Beck and Steer, 1990) and DASS-Anxiety scale (Lovibond and Lovibond, 1995). Severity of panic attacks, stress, and generalized anxiety were assessed using the Panic Disorder Severity Scale-Self Report (Houck et al., 2002), DASS-Stress subscale (Lovibond and Lovibond, 1995), and Generalized Anxiety Disorder-7 (GAD-7) (Spitzer et al., 2006), respectively. These measures have all been previously validated in similar clinical samples (Brown et al., 1997; Joiner et al., 1999; Quilty et al., 2010; Rutter and Brown, 2017).

### 2.3. Data analysis

Two-by-two contingency tables were used to determine the prevalence of comorbid disorders among depressed outpatients with and without AD. Pearson's chi-square tests (two-tailed) were used to determine if patients with AD were significantly more likely than those without AD to have a comorbid diagnosis of GAD, PD, any other *DSM-5* anxiety disorder, and any other *DSM-5* internalizing disorder (i.e., obsessive-compulsive, trauma/stress, or somatic symptom disorder). Odds-ratios (ORs) with 95% confidence intervals (CIs) were also calculated.

Hierarchical multiple regressions were used to determine if the AD specifier explained significant unique variance in functional impairment and symptom severity beyond comorbid GAD, PD, and any other anxiety or internalizing disorder. A model was estimated for each dependent variable, with dummy codes representing these four *DSM-5* disorder categories entered in the first block and a dummy code for AD entered in the second

block. Unstandardized and completely standardized solutions were examined to evaluate the significance and strength of parameter estimates. The data were analyzed in Mplus 7.1 (Muthén and Muthén, 1998). Missing data and non-normality were accommodated using robust maximum likelihood estimation (Raykov, 2005).

### 3. Results

#### 3.1. Prevalence

Two-thirds of patients (66.2%) were assigned the AD specifier (Table 1). Rates of AD were similar regardless if the depressive disorder was assigned as a principal (67.4%) or additional diagnosis (65.5%;  $\chi^2_1 = 0.09, p = .769$ ); we thus did not distinguish between principal versus additional diagnosis in the subsequent analyses of AD prevalence and associations with diagnostic comorbidity. The rate of AD among patients with MDD (70.8%) did not differ from the rate among patients with PDD (60.8%;  $\chi^2_1 = 2.63, p = .104$ ). Likewise, rates of AD did not vary across PDD longitudinal course subtypes (present among 50–70% of PDD patients across the four subtypes,  $\chi^2_3 = 2.12, p = .549$ ). Whereas roughly one-third of the sample had mild AD (i.e., exactly two symptoms, 33.07%), only a small proportion had severe AD (i.e., all five symptoms, 3.38%). Patients with MDD and PDD did not differ in frequency of the AD severity classifiers ( $\chi^2_3 = 3.90, p = .273$ ). Among the subset of patients for which symptom-level information was available ( $n = 199$ ), MDD and PDD patients endorsed each of the five symptoms at a similar frequency ( $\chi^2_1 = 0.19 - 1.61, p = .204 - .822$ ) and severity ( $t_s = 0.07 - 1.54, p = .124 - .994$ ). Difficulty concentrating because of worry was the most common (70.20%) and severe symptom (Mean = 4.00,  $SD = 2.18$ ), while feeling one might lose control was the least common (16.84%) and severe (Mean = 1.41,  $SD = 2.07$ ).

#### 3.2. Associations with comorbidity

Patients with AD were significantly more likely than those without AD to have a comorbid GAD diagnosis (OR = 2.47, 95% CI 1.42–4.29;  $\chi^2_1 = 10.53, p < .001$ ) (Table 2). This was primarily due to GAD being much more common among MDD patients with AD (66.30%) than MDD patients without AD (31.58%;  $\chi^2_1 = 13.17, p < .001$ ). In comparison, AD was not significantly associated with PD ( $\chi^2_1 = 1.06, p = .30$ ), other anxiety disorders ( $\chi^2_1 = 0.09, p = .77$ ), or other internalizing disorders ( $\chi^2_1 = 2.11, p = .146$ ). Although not statistically significant, the direction of the associations between AD and comorbid disorders was consistently in the expected direction among patients with PDD (i.e., ORs > 1.0 for all disorders). AD was inversely (but not significantly) associated with PD and other anxiety disorders among patients with MDD. Regarding total number of comorbid internalizing disorders, patients with AD were significantly more likely to have four or more comorbid disorders (OR = 3.89, 95% CI 0.99–5.66;  $\chi^2_1 = 3.89, p = .049$ ) because having four or more disorders was much more common among PDD patients with AD (21.54%) than PDD patients without AD (4.76%;  $\chi^2_1 = 5.65, p = .017$ ).

### 3.3. Incremental validity

Patients did not differ with respect to any of the dimensional dependent variables regardless of whether they were assigned a principal versus additional diagnosis of depression, or whether the diagnosis was MDD versus PDD (results available by request). The hierarchical regressions were consequently performed in the full sample. Means and standard deviations were computed for each dependent variable in the total sample as well as separately among patients with and without AD. Patients with AD had higher scores than patients without AD on all nine dependent variables (Table 3).

In Block 1 of the hierarchical regressions, GAD was significantly associated with all dependent variables ( $t_s = 1.98\text{--}4.16$ ,  $p_s = < .001\text{--}0.047$ ) except self-reported impairment and DASS-Depression (Table 4). PD was significantly associated with both measures of impairment ( $t_s = 2.31\text{--}3.48$ ,  $p_s = .001\text{--}.021$ ) and three of the five measures of anxiety symptom severity ( $t_s = 3.83\text{--}5.84$ ,  $p_s < .001$ ). Other anxiety disorders and other internalizing disorders were inconsistently associated with the dependent variables.

In Block 2, AD was significantly associated with all dependent variables ( $t_s = 2.13\text{--}6.22$ ,  $p_s = < .001\text{--}.033$ ) except clinician-rated impairment. Controlling for the four *DSM-5* disorder dummy variables, depressed patients with AD had more severe self-reported functional impairment, autonomic arousal, stress, panic, generalized anxiety, and depression than patients without AD. AD uniquely predicted between 2% (DASS-Depression) and 14% (DASS-Anxiety) of the variance across dependent variables. These incremental associations of AD with DASS-Anxiety and GAD-7 scores were of medium magnitude ( $f^2 = 0.17\text{--}0.18$ ), while the associations with DASS-Stress and the Beck Anxiety Inventory approached the medium range ( $f^2 = 0.10\text{--}0.12$ ). In comparison, the incremental associations of AD with the other dependent variables were small ( $f^2 = 0.02\text{--}0.06$ ). The sizes of the incremental associations of AD with the dependent variables were virtually identical to the sizes of the zero-order associations between AD and the dependent variables ( $R^2 < 0.02$ ; results available by request).

## 4. Discussion

This is the first study to examine the prevalence, patterns of comorbidity, and incremental validity of the AD specifier, assessed via clinical diagnostic interview, in depressed outpatients. Consistent with study hypotheses, roughly two-thirds of patients met criteria for AD. The rate of AD among patients with PDD was slightly lower but not significantly different than the rate among patients with MDD. The rates of AD observed here are slightly higher than estimates from outpatient (56%) (McIntyre et al., 2016) and mixed outpatient/community samples (54–59%) in which AD was approximated using questionnaires developed for other purposes (Gaspersz et al., 2017a, 2017b). On the other hand, AD rates in the current sample are similar to estimates (a) among outpatients with current MDD, based on a self-report questionnaire designed to assess AD symptoms in the past week (68%) (Zimmerman et al., 2014), and (b) among individuals in the general population with past 12-month MDD, based on a structured interview assessment of AD symptoms during the two-week period when depression or anhedonia were most severe (70%) (Hasin et al., 2018). The only prior study to assess whether AD symptoms were present the majority of

days with depression (via clinical interview) was conducted in a partial hospital setting and a found slightly higher rate (78%) among patients with MDD (Zimmerman et al., 2017) than was observed here. This difference is likely due to a much larger proportion of patients in the partial hospital setting endorsing a feeling that they might lose control of themselves (40%) compared to the current outpatient sample (17%), as rates of the other four AD symptoms appear generally similar across these two settings.

Gaspersz and colleagues' found individuals diagnosed with *DSM-IV*MDD with AD (assessed using proxy questionnaire items) to be more likely than those without AD to have comorbid GAD, PD, and other anxiety disorders (Gaspersz et al., 2017a). Our results indicate that MDD patients with AD are indeed more likely to have a comorbid GAD, but are *not* more likely to have comorbid PD or other anxiety disorders (non-significant ORs *below* 1.0). Similarly, AD was not significantly associated with GAD, PD, or other anxiety disorders among patients with PDD, although ORs were all *above* 1.0. Our findings may have differed from Gaspersz and colleagues' (Gaspersz et al., 2017a) because AD was assessed here using a clinical interview rather than questionnaire items developed for other purposes, or because our sample was comparatively underpowered ( $n = 237$  versus 1080). Differences could also be due to varying MDD and PDD diagnostic criteria applied across studies (i.e., *DSM-IV* versus *DSM-5*). For example, a major depressive episode lasting two or more years was classified as chronic *DSM-IV*MDD by Gaspersz and colleagues, but as PDD in *DSM-5* and the current study. Although AD was not significantly associated with comorbidity among patients with PDD in the current study, ORs were consistently above 1.0. It is possible that significant associations of AD with comorbid PD and other anxiety diagnoses may be limited to individuals with *DSM-5* PDD/chronic *DSM-IV*MDD. If true, this suggests that AD may be an indirect marker of comorbid GAD among patients with episodic depression (e.g., MDD), but a more general marker of comorbid anxiety among patients with chronic depression (e.g., PDD). Along these lines, PDD patients with AD were over five times more likely than PDD patients without AD to have four or more comorbid internalizing disorders.

AD offered incremental validity over comorbid diagnoses in predicting severity of self-reported functional impairment, autonomic arousal, stress, panic, generalized anxiety, and depression. These findings are consistent with study hypotheses and expand on prior evidence supporting the incremental validity of AD when it is assessed using proxy questionnaire items (Gaspersz et al., 2017a, 2017b). Despite controlling for comorbid PD and GAD, the strongest effects were observed between AD and measures of autonomic arousal (DASS-Anxiety, BAI) and generalized anxiety (GAD-7). These findings are somewhat surprising because autonomic arousal is a core feature of panic disorder (Brown et al., 1998; Brown and McNiff, 2009), while the GAD-7 assesses most *DSM-5* GAD symptoms (Spitzer et al., 2006). Consequently, the AD specifier may be able to identify individuals experiencing particularly severe autonomic arousal and generalized anxiety symptoms in ways not captured by *DSM-5* PD and GAD diagnoses.

Collectively, the existing literature and current study indicate that AD is a reliable and valid construct that is important for clinicians to assess when meeting patients with unipolar mood disorders. It is noteworthy that most of the comorbid disorders significantly associated



with the dependent variables in Block 1 of hierarchical regressions remained significant after adding AD to the models (Table 4). This underscores the importance of assessing both AD *and* comorbid *DSM-5* anxiety disorders when evaluating depressed outpatients. Clinicians can determine if a patient is experiencing AD using self-report or clinical interview measures (Zimmerman et al., 2017, 2014) developed specifically to assess AD symptoms. Alternatively, in addition to the ADIS-5, many other popular clinical interviews for *DSM-5* disorders include modules to assess AD symptoms (e.g., Structured Clinical Interview for *DSM* (First et al., 2015); Mini International Neuropsychiatric Interview for *DSM-5* (Sheehan, 2015). To determine the optimal method of assessing AD, additional research is needed to compare the predictive validity of self-report and clinical interview measures.

Three study limitations are noteworthy. First, the data were collected as part of an intake assessment and were thus exclusively cross-sectional. Studies using proxy questionnaire items to assess AD indicate that AD has prospective incremental validity (over *DSM-IV* disorders) in predicting the course and treatment response of *DSM-IV* MDD, but research is needed to confirm these associations using *DSM-5* criteria for AD, MDD, PDD, and comorbid disorders. Second, our sample was from a single, albeit large and relatively diverse (e.g., 25% non-Caucasian), outpatient clinic specializing in the treatment of internalizing disorders. The current findings may not generalize to all outpatient clinics, particularly given the high rates of anxiety disorder comorbidity and possibility that patients had more severe anxiety symptoms than patients seeking services at a non-specialty clinic. At the same time, there does not appear to be an inflated rate of AD in the current sample; prevalence estimates were very similar to estimates from a large non-specialty outpatient clinic and epidemiological sample with much lower rates of comorbid anxiety disorders (Hasin et al., 2018; Zimmerman et al., 2014). Third, our sample did not include patients with bipolar disorders. This is a limitation of the broader AD literature, as research has focused exclusively on AD within the context of unipolar depression.

Our findings add to a growing literature supporting the continued inclusion of AD in future editions of *DSM-5*. We found a high prevalence of AD among outpatients with MDD and PDD, evidence of differential comorbidity patterns among patients with MDD versus PDD, and support for the incremental validity of the AD specifier over and above *DSM-5* diagnoses. Although additional research is needed, the assessment of AD symptoms could aid clinicians in determining severity of functional impairment and other anxiety and depression symptoms among outpatients.

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Table 1

Frequency and severity of anxious distress specifier and symptoms.

Anxious distress <sup>a</sup>	MDD		PDD		Either MDD or PDD (Full sample)	
	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)
Any	70.77	3.29 (2.29)	60.75	3.25 (2.31)	66.24	3.28 (2.29)
Mild	37.69	2.08 (2.32)	25.23	2.10 (2.27)	32.07	2.09 (2.29)
Moderate	19.23	4.06 (2.21)	15.89	3.92 (2.16)	17.72	4.00 (2.18)
Moderate-severe	11.54	2.45 (2.40)	14.95	3.00 (2.64)	13.08	2.69 (2.52)
Severe	2.31	1.21 (1.95)	4.67	1.66 (2.19)	3.38	1.41 (2.07)
(n)	(130)	(112)	(107)	(87)	(237)	(199)
Symptoms <sup>b</sup>	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)
Feeling keyed up or tense	60.71	3.29 (2.29)	51.72	3.25 (2.31)	56.78	3.28 (2.29)
Feeling unusually restless	31.25	2.08 (2.32)	36.78	2.10 (2.27)	33.67	2.09 (2.29)
Difficulty concentrating because of worry	71.43	4.06 (2.21)	68.60	3.92 (2.16)	70.20	4.00 (2.18)
Fear that something awful may happen	43.75	2.45 (2.40)	45.35	3.00 (2.64)	44.44	2.69 (2.52)
Feeling you might lose control of yourself	15.18	1.21 (1.95)	19.05	1.66 (2.19)	16.84	1.41 (2.07)
(n)	(130)	(112)	(107)	(87)	(237)	(199)

Abbreviations: MDD, major depressive disorder; GAD, generalized anxiety disorder; PDD, persistent depressive disorder.

<sup>a</sup>Rates of anxious distress did not differ among patient with MDD and PDD ( $\chi^2_1 = 2.63, p = .104$ ), nor did rates of the four anxious distress severity classifiers ( $\chi^2_1 = 3.90, p = .273$ ).

<sup>b</sup>Symptom-level data was available for 83.4% of the sample. Patients with MDD and PDD did not differ in the frequency of anxious distress symptoms: keyed up or tense:  $\chi^2_1 = 1.61, p = .204$ ; unusually restless:  $\chi^2_1 = 0.67, p = .413$ ; concentration because of worry:  $\chi^2_1 = 0.19, p = .667$ ; fear something awful may happen:  $\chi^2_1 = 0.50, p = .822$ ; feeling might lose control:  $\chi^2_1 = 0.51, p = .474$ . Diagnosticians also made severity ratings for anxious distress symptoms using a 0 (none) to 8 (very severe) scale. Patients with MDD and PDD did not differ in severity of symptoms (df = 197): keyed up or tense:  $t = -0.127, p = .899$ ; unusually restless:  $t = 0.070, p = .944$ ; concentration because of worry:  $t = -0.457, p = .648$ ; fear something awful may happen:  $t = 1.543, p = .124$ ; feeling might lose control:  $t = 1.518, p = .131$ .

Table 2

Frequency of comorbid disorders among patients with and without anxious distress.

Comorbid disorder	(n)	Without Anxious Distress, %	With Anxious Distress, %	$\chi^2$	OR (95% CI)
MDD subsample					
GAD	(73)	31.58	66.30	13.17***	4.26 (1.90–9.58)
Panic disorder	(22)	18.42	16.30	0.09	0.86 (0.32–2.32)
Any other anxiety disorder	(71)	57.89	53.26	0.23	0.83 (0.39–1.78)
Any other internalizing disorder	(41)	28.95	32.61	0.17	1.19 (0.52–2.71)
2 + internalizing disorders	(76)	55.26	59.78	0.23	1.20 (0.56–2.58)
3 + internalizing disorders	(36)	21.05	30.43	1.18	1.64 (0.67–4.03)
4 + internalizing disorders	(20)	13.16	16.30	0.21	1.29 (0.43–3.83)
PDD subsample					
GAD	(68)	57.14	67.69	1.23	1.57 (0.70–3.51)
Panic disorder	(19)	9.53	23.08	3.21	2.85 (0.88–9.28)
Any other anxiety disorder	(77)	69.05	73.85	0.29	1.27 (0.54–2.98)
Any other internalizing disorder	(39)	26.19	43.08	3.14	2.13 (0.92–4.97)
2 + internalizing disorders	(77)	64.29	76.92	2.02	1.85 (0.79–4.36)
3 + internalizing disorders	(39)	26.19	43.08	3.14	2.13 (0.92–4.97)
4 + internalizing disorders	(16)	4.76	21.54	5.65*	5.49 (1.18–25.57)
Full sample					
GAD	(141)	45.00	66.88	10.53**	2.47 (1.42–4.29)
Panic disorder	(41)	13.75	19.11	1.06	1.48 (0.70–3.14)
Any other anxiety disorder	(148)	63.75	61.78	0.09	0.92 (0.53–1.61)
Any other internalizing disorder	(80)	27.50	36.94	2.11	1.55 (0.86–2.78)
2 + comorbid disorders	(153)	60.00	66.88	1.10	1.35 (0.77–2.35)
3 + comorbid disorders	(75)	23.75	35.67	3.48	1.78 (0.97–3.28)
4 + comorbid disorders	(36)	8.75	18.47	3.89*	2.36 (0.99–5.66)

Abbreviations: MDD, major depressive disorder; GAD, generalized anxiety disorder; PDD, persistent depressive disorder.

\* p &lt; .05.

\*\* p &lt; .01.

.100) < d  
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**Table 3**

Means and standard deviations of the correlates.

	Total sample		Without Anxious distress		With Anxious distress	
	Mean	SD	Mean	SD	Mean	SD
Overall Impairment						
Self-reported	19.13	9.72	16.00	9.96	20.77	9.20
Clinician-rated	5.75	0.79	5.58	0.81	5.83	0.77
Anxiety						
Beck anxiety inventory	21.43	11.16	16.07	9.18	24.29	11.09
DASS anxiety	7.66	4.88	4.97	3.56	9.10	4.90
DASS stress	11.29	4.40	9.32	3.85	12.33	4.32
Panic disorder severity scale	7.84	6.29	5.70	5.82	8.98	6.25
GAD-7	13.28	4.73	10.56	4.29	14.74	4.31
Depression						
Beck depression inventory	27.95	9.67	24.75	8.66	29.65	9.77
DASS depression	11.29	4.82	10.27	4.65	11.84	4.84

Abbreviations: SD, standard deviation; DASS, depression anxiety and stress scales; GAD-7, generalized anxiety disorder-7 scale.

Table 4

Incremental associations of anxious distress with functional impairment and anxiety/depression severity.

Dependent variable	B	SEB	t	B*	R <sup>2</sup>	f <sup>2d</sup>
Overall Impairment						
I. Self-reported						
<i>Block 1</i> : GAD	1.166	1.303	0.895	.059	.10*	0.12
Panic disorder	6.394	1.838	3.478***+	.248		
Any other anxiety disorder	1.756	1.351	1.299	.087		
Any other internalizing disorder	2.522	1.358	1.857	.122		
<i>Block 2</i> : Anxious distress	4.327	1.355	3.192**	.210	.15** ( = .04)	0.05
II. Clinician-rated						
<i>Block 1</i> : GAD	0.204	0.096	2.124*	.126	.17***	0.20
Panic disorder	0.297	0.128	2.313*+	.142		
Any other anxiety disorder	0.385	0.100	3.843***+	.235		
Any other internalizing disorder	0.374	0.100	3.743***+	.223		
<i>Block 2</i> : Anxious distress	0.181	0.102	1.783	.108	.18*** ( = .01)	0.01
Anxiety						
I. Beck anxiety inventory						
<i>Block 1</i> : GAD	4.326	1.441	3.002***+	.189	.17**	0.20
Panic disorder	8.346	2.034	4.103***+	.282		
Any other anxiety disorder	3.093	1.497	2.066*+	.134		
Any other internalizing disorder	2.192	1.506	1.455	.092		
<i>Block 2</i> : Anxious distress	7.312	1.451	5.041***	.309	.26*** ( = .09)	0.12
II. DASS anxiety						
<i>Block 1</i> : GAD	1.274	0.642	1.984*	.128	.13**	0.15
Panic disorder	3.458	0.903	3.829***+	.267		
Any other anxiety disorder	1.310	0.668	1.962*+	.129		
Any other internalizing disorder	0.596	0.672	0.887	.058		



Dependent variable	B	SE B	t	B*	R <sup>2</sup>	f <sup>2a</sup>
<i>Block 2:</i> Anxious distress	3.910	0.629	6.217***	.378	.26*** (= .14)	0.18
III. DASS stress						
<i>Block 1:</i> GAD	1.291	0.608	2.122*	.144	.03	0.03
Panic disorder	0.449	0.855	0.525	.039		
Any other anxiety disorder	0.266	0.633	0.420	.029		
Any other internalizing disorder	0.435	0.636	0.684	.047		
<i>Block 2:</i> Anxious distress	2.850	0.619	4.604***	.307	.12** (= .09)	0.10
IV. Panic disorder severity scale						
<i>Block 1:</i> GAD	2.051	0.788	2.604**	.159	.23***	0.30
Panic disorder	6.489	1.110	5.844*** <sub>+</sub>	.386		
Any other anxiety disorder	2.049	0.818	2.506* <sub>+</sub>	.156		
Any other internalizing disorder	0.283	0.823	0.344	.021		
<i>Block 2:</i> Anxious distress	2.885	0.814	3.543***	.215	.28*** (= .05)	0.06
V. GAD-7						
<i>Block 1:</i> GAD	2.186	0.627	3.486*** <sub>+</sub>	.227	.11**	0.12
Panic disorder	1.641	0.882	1.860	.131		
Any other anxiety disorder	1.056	0.652	1.619	.108		
Any other internalizing disorder	1.289	0.656	1.965*	.129		
<i>Block 2:</i> Anxious distress	3.700	0.618	5.991***	.371	.24*** (= .13)	0.17
Depression						
I. Beck depression inventory						
<i>Block 1:</i> GAD	5.237	1.260	4.155*** <sub>+</sub>	.267	.14**	0.16
Panic disorder	-1.649	1.778	-0.927	-.065		
Any other anxiety disorder	5.220	1.309	3.988*** <sub>+</sub>	.262		
Any other internalizing disorder	0.670	1.316	0.509	.033		
<i>Block 2:</i> Anxious distress	3.946	1.315	3.000**	.194	.17*** (= .03)	0.04
II. DASS depression						
<i>Block 1:</i> GAD	0.478	0.668	0.716	.049	.02	0.02
Panic disorder	0.560	0.938	0.597	.044		

Dependent variable	B	SE B	t	B*	R <sup>2</sup>	f <sup>2a</sup>
Any other anxiety disorder	1.196	0.695	1.721	.120		
Any other internalizing disorder	0.186	0.699	0.266	.018		
Block 2: Anxious distress	1.503	0.704	2.134*	.148	.04 ( = .02)	0.02

Abbreviations: DASS, depression anxiety and stress scales; GAD-7, generalized anxiety disorder-7 scale.

<sup>a</sup>The top value for Cohen's  $f^2$  represents the overall model effect size for the four DSM-5 disorder categories. The bottom value reflects the effect size only for anxious distress (not the full model).

\* p < .05.

\*\* p < .01.

\*\*\* p < .001.

<sup>†</sup>Block 1 variable remained significant after adding anxious distress to the model.