Mixed Anxiety Depression Should Not Be Included in DSM-5
Batelaan, N.M.; Spijker, J.; de Graaf, R.; Cuijpers, P.

published in
Journal of Nervous and Mental Disease
2012

DOI (link to publisher)
10.1097/NMD.0b013e318257c4c9

document version
Publisher's PDF, also known as Version of record

Link to publication in VU Research Portal

citation for published version (APA)

General rights
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

• Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying the publication in the public portal

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:
vuresearchportal.ub@vu.nl

Download date: 12. Apr. 2022
Mixed Anxiety Depression Should Not Be Included in DSM-5

Neeltje M. Batelaan, MD, PhD,*† Jan Spijker, MD, PhD,‡§|| Ron de Graaf, PhD,‡ and Pim Cuijpers, PhD†¶

Abstract: Subthreshold anxiety and subthreshold depressive symptoms often co-occur in the general population and in primary care. Based on their associated significant distress and impairment, a psychiatric classification seems justified. To enable classification, mixed anxiety depression (MAD) has been proposed as a new diagnostic category in DSM-5. In this report, we discuss arguments against the classification of MAD. More research is needed before reifying a new category we know so little about. Moreover, we argue that in patients with MAD symptoms and a history of an anxiety or depressive disorder, symptoms should be labeled as part of the course trajectories of these disorders, rather than calling it a different diagnostic entity. In patients with incident co-occurring subthreshold anxiety and subthreshold depression, subthreshold categories of both anxiety and depression could be classified to maintain a consistent classification system at both threshold and subthreshold levels.

Key Words: Anxiety, classification, depression, diagnosis, mixed anxiety depression.

© 2012 Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

Depressive and anxiety symptoms are extremely common in the general population and in primary care (Batelaan et al., 2007; Cuypers et al., 2004; Katon and Roy-Byrne, 1991; Olsson et al., 1996; Ormel et al., 1993; Rucci et al., 2003; Zimbarg et al., 1994), and they frequently co-occur (Das-Munshi et al., 2008; Piccinelli et al., 1999; Preissig et al., 2001; Spijker et al., 2010). Co-occurring subthreshold depression and subthreshold anxiety are associated with impaired functioning (Das-Munshi et al., 2008; Preissig et al., 2001; Roy-Byrne et al., 1994). For example, one fifth of work loss days occurred in those with co-occurring subthreshold depression and subthreshold anxiety (Das-Munshi et al., 2008). Moreover, seeking treatment is common in this group, suggesting significant levels of distress (Preissig et al., 2001; Roy-Byrne et al., 1994). For example, of those with comorbid subthreshold anxiety and subthreshold depression, as diagnosed on a lifetime basis, 63% had ever sought treatment for their complaints (Preissig et al., 2001). Individuals with co-occurring subthreshold anxiety and subthreshold depression lack a specific psychiatric diagnosis in the DSM-IV classification system, whereas a psychiatric classification may be justified based on the associated significant distress or associated impairment.

To enable classification of those with co-occurring subthreshold anxiety and subthreshold depression, a distinct diagnosis has been proposed. Since 1992, classifying mixed anxiety and depressive disorder is possible using the ICD-10 classification system (World Health Organization, 1992). However, in ICD-10, the criteria have not been defined very precisely. According to the ICD-10, the category of Mixed Anxiety and Depressive Disorder should be used when symptoms of anxiety and depression are both present, but neither is clearly predominant, and neither type of symptom is present to the extent that justifies a diagnosis if considered separately. When both anxiety and depressive symptoms are present and severe enough to justify individual diagnoses, both diagnoses should be recorded and this category should not be used” (World Health Organization, 1992). The appendix of the DSM-IV included research criteria for mixed anxiety–depressive disorder that are more specific (Table 1) (American Psychiatric Association, 1994). Recently, criteria have been proposed to be included in DSM-5 using the term mixed anxiety depression (MAD) (American Psychiatric Association, 2012a). For DSM-5, the draft diagnostic criteria of MAD read as follows. Three or four of the symptoms of major depression must be present, which must include depressed mood and/or anhedonia. These symptoms should be accompanied by anxious distress, defined as having two or more of the following: irrational worry, preoccupation with unpleasant worries, having trouble relaxing, motor tension, and fear that something awful may happen. Symptoms must have lasted at least 2 weeks, are occurring at the same time, and no other DSM diagnosis of anxiety or depression must be present (American Psychiatric Association, 2012a) (Table 2). These criteria are still tentative. For example, it has not been decided whether the minimum number of required depressive symptoms should be three or four. Field trials investigating the feasibility, clinical utility, and reliability of the draft criteria of MAD have been conducted. The proposed criteria may be revised after the field trials (American Psychiatric Association, 2012b).

Slightly different names have been used for this disease concept. For reasons of clarity, the term mixed anxiety depression (MAD) will be used throughout this article.

Including such a diagnosis in DSM-5 may have several advantages. A diagnosis of MAD may raise awareness about the frequent co-occurrence of subthreshold anxiety and depression and its clinical and public health significance. Moreover, it would provide the opportunity to investigate the prevalence, consequences, and course while using standardized criteria. By facilitating research, the development of (cost-) effective treatment strategies may be accelerated, as a result of which the burden of disease generated by MAD could be reduced. Finally, the DSM classification system would be more compatible with the ICD classification system, although the definitions of these two entities remain divergent. Although acknowledging that co-occurring subthreshold anxiety and depression warrant clinical attention, we seriously question whether including MAD in the classification system of the DSM-5 is the most rational and valid option available. On the basis of previous research, we discuss several concerns regarding the concept of MAD: a) divergent results of previous research, b) inconsistency in nomenclature between subthreshold and threshold level, and c) limited diagnostic stability over time.

DIVERGENT RESULTS OF PREVIOUS RESEARCH

MAD has been investigated using different sets of criteria, and as a result, previous results on prevalence and course have been
requirement in the DSM-5 criteria to consider the context in which the depressive and anxiety symptoms arose. Many stressful life events may trigger anxiety and depressive symptoms that meet the 2-week duration criterion for MAD, many of which are likely to be a transient and normal response to these stressful life events and thus constitute false-positives if the diagnosis of MAD were applied.

At the time of including MAD in the Appendix of DSM-IV in 1994 (American Psychiatric Association, 1994), Zinbarg et al. (1994) stated that the sensitivities and specificities associated with different symptom thresholds should be investigated, as well as the prevalence in the general population. We think that this statement still holds true: given the substantial impact of criteria on prevalence, the limited clinical utility in case of low prevalence rates, and the potentially adverse consequences in case of many false-positives, these issues should be addressed before including MAD in DSM-5. Although MAD is on the list of proposed disorders to be investigated in field trials in large academic clinic settings (American Psychiatric Association, 2012b), answering the questions above require investigating MAD in both primary care settings or the general population, neither of which are included in the DSM-5 Field Trial samples.

INCONSISTENCY IN NOMENCLATURE BETWEEN SUBTHRESHOLD AND THRESHOLD LEVELS

Anxiety and depression are highly comorbid at both subthreshold and threshold levels (Das-Munshi et al., 2008; De Graaf et al., 2002; Kessler et al., 2005, 1994; Piccinelli et al., 1999; Preissig et al., 2001; Spijker et al., 2010), anxiety disorders and depressive disorders share a genetic vulnerability (Hettema et al., 2006), and diagnostic conversions occur over time from anxiety disorders to depressive disorders and vice versa (Hagnell and Grasbeck, 1990; Merikangas et al., 2003; Rhebergen et al., 2011). These findings have raised the fundamental question of whether it is justified to regard anxiety and depressive disorders as different disease concepts. Previously, a tripartite model of anxiety and depressive disorders has been postulated (Clark and Watson, 1991), consisting of anxiety, depression, and MAD. According to this model, anxiety and depression share the presence of nonspecific general distress or negative affect. In addition, the lack of positive affect is specific to depression and the presence of hyper arousal to anxiety. According to this model, MAD is predominantly characterized by the presence of nonspecific general distress. In line with this, a profile analysis has shown that subclinical patients most often had a nonspecific symptom profile (Barlow and Campbell, 2000). However, previously, we have found little differences between MAD, pure subthreshold anxiety, and pure subthreshold depression in terms of sociodemographics, care utilization, functioning, and 2-year course (Spijker et al., 2010). Thereby, the benefits of classifying MAD over classifying both subthreshold anxiety and subthreshold depression can be questioned. It will be possible to classify subthreshold depression in DSM-5 using the term Subsyndromal Depressive CNEC, a subcategory of “Depressive Conditions Not


<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
</table>
| The patient has three or four of the symptoms of major depression (which must include depressed mood and/or anhedonia), and they are accompanied by anxious distress. The symptoms must have lasted at least 2 weeks, and no other DSM diagnosis of anxiety or depression must be present, and they are both occurring at the same time.

Anxious distress is defined as having two or more of the following symptoms: irrational worry, preoccupation with unpleasant worries, having trouble relaxing, motor tension, fear that something awful may happen.
Limited Diagnostic Stability over Time

At the time of conducting the DSM-IV field trials for MAD, it was acknowledged that the validity of MAD needed further study (Zinbarg et al., 1994). To validate a disease concept, diagnostic stability over time is regarded as important: “a rose is a rose because it remains a rose” (Goodwin and Guze, 1996). This implies that prodromal symptoms, symptoms in the context of a disorder, and residual symptoms after remission of the disorder should all be captured within the same disease concept. However, the disease concept of MAD appears to include a rather heterogeneous group of patients.

Previously, it was mentioned that the possibility that MAD is a prodromal stage of MDD or generalized anxiety disorder needed to be ruled out (Zinbarg et al., 1994). That is, if MAD appears to be a prodromal stage of another psychiatric disorder, MAD should be better regarded a prodromal stage of this disorder rather than calling it a different diagnostic concept. Previous research has shown that in primary care, almost half of those with MAD at baseline had developed a threshold psychiatric disorder after a 1-year follow-up (Barkow et al., 2004). Thus, MAD was a prodromal stage in about half the cases. Of note, 27% had developed a depressive disorder, dysthymia, agoraphobia, panic disorder, or comorbid anxiety and depressive disorder, whereas another 22% fulfilled criteria of another ICD-10 disorder such as pain disorder, somatization disorder, hypochondriasis, or alcohol disorders (Barkow et al., 2004). In addition, the results of a taxometric analysis reported the development of anxiety and depressive disorders over time (Schmidt et al., 2007). In the rationale accompanying the proposed revisions on the DSM-5 Web site, the progression to full-blown psychiatric disorders is used as an argument to establish MAD as a diagnostic category in DSM-5 (American Psychiatric Association, 2012a). In our opinion, the progression of MAD to full-blown disorders suggests that its course may be unfavorable and that the condition may therefore warrant attention, but it does not mean that establishing MAD as a separate diagnostic category is the best way to call attention to the condition. Given that at the time of presenting with MAD symptoms, the specific future disorder is not known, subthreshold anxiety and subthreshold depression could be classified instead. Second, limited diagnostic stability has been reported when reassessing those with MAD over time. Several studies reported almost no cases with MAD at baseline that still fulfilled criteria of MAD at follow-up (Barkow et al., 2004; Spijker et al., 2010). Third, some previous findings suggest that a substantial proportion of those with “MAD” experience MAD symptoms in the waxing and waning course of a threshold depressive disorder or threshold anxiety disorder. Roy-Byrne et al. (1994) reported that 95% of the individuals with subthreshold symptoms in primary care have a lifetime history of depression (OR, 4.0), a recent history of depression (OR, 4.8), a lifetime history of panic disorder (OR, 4.6), or a recent history of panic disorder (OR, 3.7) in primary care patients with mixed subthreshold anxiety and subthreshold depression. To ensure that MAD as a diagnostic category would not contain residual symptoms of threshold anxiety and depressive disorders, those with a current anxiety or depressive disorder and those with a history of an anxiety disorder (i.e., panic disorder or generalized anxiety disorder) or depressive disorder (i.e., major depressive disorder or dysthymic disorder) were excluded according to the research criteria of the DSM-IV (American Psychiatric Association, 1994) (Table 1). Whereas Zinbarg et al. (1994) reported little impact of these exclusion criteria, we found that applying these exclusion rules resulted in very low annual prevalence rates of 0.6% for MAD. Moreover, applying these exclusion criteria may select a less severe group that may not fulfill criteria of clinical relevance, as suggested by the limited consequences in terms of functioning, care utilization, and course when applying these exclusion rules (Spijker et al., 2010). Those with a history of an anxiety or a depressive disorder are no longer to the proposed criteria of DSM-5, suggesting that those with MAD according to the proposed criteria of DSM-5 consist of a heterogeneous group of patients including many with either prodromal symptoms or residual symptoms occurring in the long-term course of threshold disorders.

Conclusion

A distinct diagnosis of MAD has been proposed to enable classification of patients with co-occurring depressive and anxiety symptoms. Although acknowledging several advantages of a distinct classification, we argue against the proposed category of MAD for several reasons. We pointed out that diagnostic criteria applied have a substantial impact on the prevalence rate. We also argued that creating such a diagnosis is inconsistent with current nomenclature in which such a comorbid diagnosis is absent at threshold level and that evident advantages of classifying MAD over classifying subthreshold categories are unclear. Finally, we questioned the validity of the proposed category based on low diagnostic stability over time.

MAD is on the list of disorders to be investigated in field trials in large academic clinic settings (American Psychiatric Association, 2012b). Although this provides the opportunity to increase knowledge on several important issues, assessing the prevalence requires studies in primary care or the general population too. Moreover, the field trials include only one follow-up evaluation after 4 to 12 weeks. Assessing diagnostic changes over time to gain insight into the validity of the MAD concept requires longer follow-up studies.

In conclusion, thorough research is needed before considering to adopt the diagnosis MAD in DSM-5. Moreover, in patients with a history of an anxiety disorder or depressive disorder, adopting a longitudinal perspective is more rational. Thus, rather than calling it a different diagnostic entity, attention should be paid to the early signs of recurrences and to long-term fluctuations in symptom level of anxiety and depressive disorders, thus labeling these symptoms as part of the course trajectories of the anxiety or depressive disorder. In patients without previous anxiety disorder and depressive disorder who present with co-occurring anxiety and depressive symptoms of clinical relevance, these symptoms could be classified as (both) subthreshold depression and subthreshold anxiety (i.e., Subsyndromal Depressive Condition Not Elsewhere Classified and Unspecified Anxiety Disorder). In doing so, a consistent classification system at both threshold and subthreshold levels will be maintained.

Disclosure

This article was written on the invitation of the Editor. It has not been financially supported: there are no acknowledgments and no disclosures related to this article.
REFERENCES


