Adjustment Disorders: A diagnosis whose time has come

Rahel Bachem and Patricia Casey (joint first authors)

Abstract

Background: Adjustment disorder is among the most frequently diagnosed mental disorders in clinical practice although it has received little academic attention and been the subject of substantial criticism over the past decades. While those suffering with adjustment disorders are often treated by mental health professionals, research interest in the origin of the disorder or the effectiveness of psychotherapeutic and medical interventions has only recently begun to emerge. This article summarizes the empirical literature published on adjustment disorder and points out current diagnostic developments in DSM-5 and ICD-11. **Methods**: Literature for this review was identified through established online search tools, including publications in English, German, and Spanish. **Results**: This paper reviews literature on the evolution of adjustment disorder, and highlights the current state of research with regard to genesis and treatment. Importantly, for the first time ICD-11 intends to define adjustment disorder by explicit symptom groups, unlike DSM-5. **Limitations**: Publications without an English abstract were not included. **Conclusions**: Key directions for future research include investigating the concordance of the ICD-11 and DSM-5 concepts and the effect that the diverging conceptualizations may have. Risk and protective factors specific to AD should be identified and the biological underpinnings of the disorder should be explored. Finally, given the high prevalence of AD in certain clinical settings effective disorder-specific interventions should be developed and evaluated.

Author Note

Rahel Bachem, PhD, Bob Shapell School of Social Work, University of Tel Aviv, Chaim Levanon 30, Tel Aviv, 699780, Israel; Prof. Patricia Casey, University College Dublin; School of Medicine; Mater Misericordiae Hospital; 62/63 Eccles Street, Dublin 7.

Correspondence should be addressed to Rahel Bachem, PhD, Bob Shapell School of Social Work, Univeristy of Tel Aviv, Chaim Levanon 30, Tel Aviv, 699780, Israel.
E-mail: rahel.bachem@gmail.com
Telephone: +972 539539542

Introduction

Adjustment disorder (AD) raises philosophical and conceptual issues that penetrate to the core of psychiatry. How does psychiatric illness differ from normal sadness or demoralisation? Can the various diagnostic syndromes be distinguished from each other? Are these naturally occurring entities or are they constructs that require testing? Some of these issues will be discussed in this paper with particular reference to the criteria proposed for ICD-11 and in use in DSM-5. This review summarizes the empirical literature published on AD and gives an overview of the current status of AD conceptualization, diagnostics and interventions.

AD is a diagnosis that attempts to encapsulate the reality that all individuals experience stressful life events and some may be so severely affected that their level of distress and incapacity effects their day to day functioning. This imposes a major personal, social and financial burden on society (Arends et al., 2012; Catalina-Romero et al., 2012). Over time most will recover and return to their former level of wellbeing. While the idea of short term, excessive stress responses has face validity, diagnoses must also have utility (Jablensky, 2016). This was confirmed in a global sample of nearly 5000 psychiatrists, where AD was identified as the seventh most frequently diagnosed mental disorder and was even more frequently used by psychologists (Evans et al., 2013; Reed et al., 2011). At the same time it was rated the fifth most problematic because of constraints between the fit of the vague criteria and clinical practice (Reed et al., 2011), which has resulted in its neglect in academic and research circles (Casey et al., 2001).

Search strategy and selection criteria

References for this review were identified through searches of PsycINFO, PubMed/Medline and Google Scholar for articles using the terms "adjustment disorder(s)" either in the title or the abstract. The focus is on articles published between 1980, when the term "Adjustment Disorder" was introduced into DSM-III, until August 2017. Earlier terms for AD (transient situational personality disorder, transient situational disturbance) were not included in the search strategy. Publications were included in the literature review if they investigated AD as their

primary focus of interest. Regarding AD treatment, single case studies and trials without a control group were excluded. Articles resulting from these searches and relevant references cited in those articles were reviewed. We included articles published in English, German, and Spanish.

Criteria for AD

Currently there are no specific symptom criteria for making a diagnosis of AD. There is a requirement that the symptoms are preceded by a stressful event closely proximal in time to the onset of symptoms. They must not reach the number, combination or duration threshold for another condition and thus AD has the status of a subthreshold disorder (e.g., Baumeister and Kufner, 2009; Casey, 2014; Hund et al., 2016). The symptoms resolve when the stressor is removed or a new level of adaptation is reached. The current criteria for AD in ICD-10 (World Health Organization, 1992) and DSM-5 (American Psychiatric Association, 2013) are summarised in panel 1. A number of subtypes are included e.g. depressed, anxious, behavioural change and mixed states.

Panel 1. Summary of ICD-10 and DSM-5 criteria for AD

AD occurs

- In response to a stressful event
- The onset of symptoms is within 3 months of exposure to the stressor and DSM and 1 month in ICD
- The symptoms must be clinically significant in that
    - they are distressing and in excess of what would be expected following exposure to the stressor

      or

    - there is significant impairment in social or occupational functioning (this is mandatory in ICD)
- The symptoms are not due to another axis 1 disorder (or bereavement in DSM)
- Once the stressor or its consequences is removed, the symptoms resolve within 6 months

Symptoms may be acute or chronic in DSM-5 (<6 months or >/= 6 months) or in ICD brief or prolonged (< 1 month or < 2 years)

The difficulties stemming from the criteria as currently constituted have been the subject of criticism by the detractors (e.g., Fabrega and Mezzich, 1987; Grassi et al., 2007) and advocates (e.g., Baumeister et al., 2009; Casey et al., 2001) of the AD concept. These include the failure to differentiate it from normal adaptive stress responses, the failure to differentiate it from other common disorders such as major depression/depressive episode, the fact that it is a default diagnosis made when the criteria for another are not met, the absence of any specific symptoms criteria to assist the clinician and the poorly validated subtypes (Baumeister et al., 2009). Many of these problems stem from the historical roots of AD.

History and evolution of AD

When the rubric "adjustment disorder" was introduced into DSM-III (American Psychiatric Association, 1987) it was as a catchall for symptoms that did not reach the threshold for more definitive disorders such as major depression (MDD). This allowed for the reimbursement of treating clinicians who otherwise would not have been. Some were scathing in their attacks arguing that AD was a pragmatic fabrication that medicalised problems of living (Fabrega and Mezzich, 1987).

Prior to the use of the AD term, different labels were used (panel 2) in the DSM and ICD classifications (American Psychiatric Association, 1980, 1952; World Health Organisation, 1978) to capture the idea that certain people react adversely to stressors in the short term.

Panel 2 History of AD in the classification systems

DSM	ICD
DSM-I (1952) Transient situational personality disorder DSM-II (1968) Transient situational disturbance DSM-III (1980) Adjustment disorder DSM-IIIR (1987) Aetiological criterion changed from psychosocial stressor to stressor DSM-5 (2014) moved from stand-alone category to Trauma and Stressor Related Disorders chapter	ICD-9 (1978) Transient situational disturbance (two subgroups – acute reactions to stress and adjustment disorders) ICD-10 (1992) Adjustment disorder

Despite minor alterations in the labels, AD never achieved the status of a full threshold disorder with its own criteria. This limited academic interest. In contrast, MDD, a term incorporated into DSM-III at the same time as AD, became a magnet for researchers (Parker, 2005). The fact of AD being a spontaneously resolving disorder also made research more challenging particularly into its psychobiology and treatment.

The final step in its evolution within DSM was the move into the new *Trauma and Stress Related Disorders* chapter in DSM-5 (American Psychiatric Association, 2013). In ICD-9 (World Health Organisation, 1978) adjustment reaction was a stand-alone disorder and in ICD-10 (World Health Organization, 1992) it became adjustment disorder in the Neurotic, Stress-Related and Somatoform Group.

Controversies

Normal stress, abnormal stress and the false positive problem

One of the difficulties with the AD diagnosis is that the distinction from normal stress reactions is unclear. There should be clear lines of demarcation between normal emotional responses and those that are pathological. These points of cleavage, referred to as "zones of rarity" (Kendell and Jablensky, 2003, p. 6), manifest themselves by differences in symptoms, biology, aetiology, natural history and so on. It was envisaged by the architects of DSM-IV (American Psychiatric Association, 1994) that over time clear biological and other distinctions would emerge, to enable delineation of disorder and non-disorder. This has not happened. This raises the spectre of psychiatric diagnoses being made on the basis of distress symptoms alone, prompting accusations that problems of living are being medicalised, an issue raised by the early critics of AD (Fabrega and Mezzich, 1987). Since there are few areas of life in which we have knowledge of the appropriate response to a particular stressor (with the possible exception of bereavement) deciding on what is a normal and what is excessive is a clinical one with little to guide the clinician.

In general medicine a binary model is applied (with a few exceptions such as hypertension and obesity where there is a continuum) since a disease like pancreatitis is either present or absent because of qualitative differences between normal and pathological tissue. Applied to psychiatry the binary model leads to the assumption that there are qualitative differences between normal and pathological sadness. There have been no studies comparing normal sadness with the emo-

tion of "depression" described in AD. However, proxy measures of normal sadness or demoralisation have been compared to the mood state of MDD. The results are conflicting with some identifying qualitative differences (Clarke and Kissane, 2002; Gutkovich et al., 1999) and others not (Costello and Healy, 1993). This approach could potentially be applied to AD also although finding nuanced terminology to capture the variety of personal mood states is difficult. Instead we are still using coarse descriptors, symptom numbers and their duration to make diagnoses in psychiatry, as the vignette (panel 3) will illustrate.

Panel 3. Case vignette illustrating the complexity of diagnosis in stress related disorders

Three weeks ago a woman discovered that her husband was a gambler and owed £30,000 to money lenders from whom he had been borrowing to sustain his habit. Since then she has been experiencing initial insomnia most nights, she is tearful and feels low in mood, she is overeating and she has withdrawn from social contacts because she cannot afford to socialise with her friends. She is unable to concentrate as she is preoccupied by what has happened. She sees the future as uncertain because she has no means of earning extra money and she becomes anxious when she hears a knock on the door fearing debt collectors. She had to take a week off work as a sales assistant initially but has now returned. She has no prior history. She attended her GP who prescribed a hypnotic and referred her for counselling. She attended one session. After two and a half weeks she was able to discontinue the hypnotic but she continues to be upset by her situation. Her mother helps her cook for her children a few hours each week because she knows she is upset. She has sought help for her husband's gambling and has made an appointment to get financial advice from a voluntary group providing such assistance to those in financial difficulties. She has notified the police that she is fearful of debt collectors.

Comment: The vignette illustrates many issues that will be discussed in relation to adjustment disorder and the failure to provide guidance on how to diagnose AD.

1. The starting point is to decide if she has a psychiatric disorder or if her symptoms are within the bounds of a normal reaction?
2. If her response is excessive what is the diagnosis?
3. Is it likely to be similar using the DSM-5 and the ICD 10 or 11 criteria?

The danger of labelling appropriate distress as disorder, perhaps AD or MDD, is known as the false positive problem. In psychiatry, this is grounded in the belief that phenomena constituted by symptom numbers and their duration define naturally occurring, discrete entities that we

refer to as psychiatric illnesses. This binary model, useful in medicine, is simplistic and procrustean when applied to psychiatry. It carries the risk that diagnosis is a "tick box" exercise that quantifies symptom numbers as feared by some (McHugh and Slavney, 2012), rather than a rounded evaluation of the individual, the context and the culture in which the symptoms developed.

Spitzer attempted to reduce the false positive risk by requiring either clinically significant distress or functional impairment to define psychiatric disorder in DSM-III (Spitzer and Wakefield, 1999). But there is no guidance on how to decide what is clinically significant and its critics of regard it as too subjective (Frances, 1998). As illustrated in panel 4, a further problem is the requirement for symptoms OR impairment but not both in DSM-5 (American Psychiatric Association, 2013) whereas ICD-10 (World Health Organization, 1992) presently requires both, thus setting the bar higher from making a diagnosis.

Panel 4. Comment 1– normal or adverse reaction?

It is clear that this lady experienced a major stressor and is exhibiting symptoms that most people in such circumstances might experience.

She had impairment in functioning for one week as she was unable to go to work but she did return then and no difficulties were reported but her mother still helps her for a few hours each week. Does she meet the functional impairment criterion required by ICD-10? Her inability to socialise was not due to her mood but because she could not afford to.

Her symptoms might meet the clinical significance criterion for distress since she required hypnotics for just over 2 weeks after which she discontinued them and she was also referred for counselling. On the other hand short term hypnotics are often prescribed for those experiencing normal stress reactions e.g. bereavement. There is also a cultural tendency to refer people for counselling when emotional symptoms are presented. This illustrates the problem with defining "clinical significance".

If the DSM-5 criteria applied (symptoms or impairment), the absence of functional impairment would be irrelevant and the decision would rest upon whether the continuing symptoms reached the clinical significance threshold, for which she required medication and counselling. Thus she would likely be diagnosed with a psychiatric illness. The question is whether it would be MDDD or AD or some other subthreshold disorder?

If ICD-10 criteria (symptoms and impairment) were applied the fact that, despite her symptoms, her functional impairment was brief, for one week only and thereafter she required help from her mother for a few hours. This would direct the clinician towards deciding that her reaction may not constitute a psychiatric disorder.

Distinguishing AD from other sub-threshold disorders

AD have been determined as "too broad to be clinically helpful" due to their considerable overlap with subthreshold manifestations of other distress disorders (Semprini et al., 2010, p. 382). For example, individuals suffering from AD due to a medical condition often show defined syndromes such as somatization, demoralization, or alexithymia concurrently. Thus, the question has been raised whether an AD diagnosis adds clinical information per se or whether it should be abandoned in favour of the more specific syndromes (Grassi et al., 2007). In consequence, two questions should be asked regarding the sub-threshold status of AD: How does it relate to other sub-threshold disorders? Should it remain in this hinterland between normal and full threshold disorders?

Sub-threshold disorders are defined as having some but not all the required criteria to make a full syndromal diagnosis. They may represent conditions in evolution, in resolution or temporary conditions that resolve spontaneously, like AD. As they are measured at a single time point their trajectory is clinically unclear. Yet they come within the provenance of psychiatry with recommendations that antidepressants should be used in their treatment (Ayuso-Mateos et al., 2010). MDD is conceptually different from AD which is based on both aetiology and long-term course while sub-threshold disorders are based on cross-sectional symptom numbers and their duration. Recent findings suggest that AD may be a chronic condition in approximately one-third of the cases (O'Donnell et al., 2016) though further studies are required to determine trajectories of AD.

The terminology of sub-threshold disorders showed huge heterogeneity in a systematic review (Rivas Rodríguez et al., 2012). For example, "sub-threshold depression" was defined as depressed mood or loss of interest but having less than five symptoms or not reporting significant impairment while "subsyndromal symptomatic depression" was defined as any two or more simultaneous symptoms of depression, present for most or all of the time, at least two weeks in duration, associated with evidence of social dysfunction. "Minor depression" was defined as not more than

4 symptoms for 2 weeks. AD was not examined in this study. The clinical application of these and their implications is demonstrated in the comment on the vignette in panel 5.

Panel 5. Comment 2 – which subthreshold disorder?

Based on the definitions of subthreshold disorders above, this lady might be diagnosed as having minor depression, subsyndromal symptomatic depression or, if aetiology was considered, AD (using DSM-5 criteria). These labels have treatment implications with psychological treatments and/or antidepressants being suggested as possible interventions to prevent the transition to a full threshold depressive disorder for subthreshold disorders (26). For AD "watch and wait" would be preferred. The label also has implications for prognosis that may affect insurance cover since one has the potential to develop into a more serious condition such as major depression while the other, AD, is self-limiting.

The second question is whether AD should remain a sub-threshold disorder. By definition this is less severe than a full threshold condition (Friedman et al., 2011) but the research does not support this view. Some studies have found no difference in symptom severity or functioning between depressive episode and AD (Casey et al., 2006) and even those that have identified statistical differences in some measures still place AD in the moderate range of symptom severity (Doherty et al., 2014; Fernández et al., 2012). There is also evidence that in some cultures AD is the most common diagnosis in both adults (Manoranjitham et al., 2010) and adolescents (Lönnqvist et al., 1995) dying by suicide. Individuals diagnosed with AD had 12 times the rate of suicide than those without an AD (Gradus et al., 2010). At present symptom clustering and differences from depressive episode in severity are being examined using much larger samples (Casey, 2017) and more advanced statistical analysis. AD patients reported significantly lower quality of life and more anxiety and depression than healthy individuals. However, those suffering from other psychiatric disorders reported higher impairment on these measures (O'Donnell et al., 2016). Nevertheless, in their totality, these finding suggest that the severity of AD warrants full threshold status.

Distinguishing AD from other psychiatric disorders

The third boundary dispute is distinguishing between AD and other disorders such as MDD/depressive episode, generalized anxiety disorder or even personality disorder and psychosomatic conditions. Within psychiatry generally there is much symptom overlap between the various common mental disorders and even between psychotic disorders. So this is not unique to AD though only adjustment disorder is conceptualized as an exclusion disorder that

cannot be assigned in combination with another full-threshold disorder (American Psychiatric Association, 2013; World Health Organization, 1992). As Stein et al. (2013, p. 2) write, these differences are characterised by "fuzzy boundaries with multiple interacting causes acting on multiple brain mechanisms".

But if conditions overlap there is likely to be diagnostic confusion and conflation, a concern identified by others (Reed et al., 2011) who found matching the limited diagnostic criteria of AD to the clinical picture problematic. There is clear evidence of this conflation from a number of studies that used a combination of clinical and research diagnoses for AD. A US study of intake assessments at a rural clinic identified 36% as having AD while only 11% were so diagnosed using SCID (Shear et al., 2000). In another study of those presenting because of self-harm, a clinical diagnosis of AD was made in 31.8% and MDD in 19.5% but a SCID interview resulted in a reversal to 7.8% versus 36.4% with MDD (Taggart et al., 2006). A further study examining AD and depressive episode in liaison psychiatry using clinical diagnosis and the SCAN instrument found a fair to poor level of concordance (Doherty et al., 2014). The sensitivity and specificity of SCAN, as the benchmark in diagnosing AD compared to clinical diagnosis, were 91.8% and 57.2% respectively. If symptoms do not adequately separate AD from MDD/depressive episode or psychosomatic disorders, are there other features that distinguish one from the other? It has been shown that suicidal behavior occurs earlier in the course of AD compared with MDD (Polyakova et al., 1998), suicidal ideation occurs at a lower symptom threshold in patients with AD (Casey et al., 2015) and the interval from suicidal threats to suicide is shorter in those with AD compared to MDD (Runeson et al., 1996). On the other hand measures of suicide intent do not distinguish the groups (Casey et al., 2015). Finally, the course of AD over time is also different with shorter time to symptom resolution and earlier return to work (Greenberg et al., 1995) and lower re-admission rates (Jones et al., 2002).

Panel 6. Comment 3 – AD or MDD?

Based on the DSM-5 criteria this lady would not be diagnosed with MDD since she has 4 and not 5 of the 9 core symptoms for over two weeks. If she had another symptom, or if the assessor regarded her social withdrawal as a symptom (rather than a financial necessity) she would pass the symptom number threshold for a diagnosis of MDD provided they were deemed to be of clinical significance (see panel 4 above for discussion of this).

If she did reach the symptom threshold and taking into account the context in which her symptoms, is MDD a reasonable diagnosis at the 2 week time point?

If AD were accorded full threshold status she would, even with 5 symptoms, be diagnosed with AD since the trigger and course over time would determine the diagnosis.

A Radical Proposal for ICD-11

In ICD-11 a radical change will take place if the proposed changes are accepted, that will create a clear, irreconcilable severance between it and DSM-5 (Maercker et al., 2013a, 2013b). These will move AD from a subthreshold disorder into a full syndrome with specific diagnostic criteria rather than the narrative description of a subthreshold disorder contained in both the DSM and ICD classifications to date (American Psychiatric Association, 2013; World Health Organization, 1992). The criteria that have been suggested for an ICD-11 research diagnosis of AD are listed in panel 7.

Panel 7. Proposed criteria for an ICD-11

1) Presence of an identifiable stressor(s) or life change(s)

2) Occurrence of symptoms of preoccupation related to the stressor in the form of at least one of the following:
   2a) excessive worry about the stressor

   2b) recurrent and distressing thoughts about the stressor

   2c) constant rumination about the implications of the stressor

3) Failure to adapt to the stressor that causes significant impairment in personal, family, social, educational, occupational or other important areas of functioning.

4) Symptoms usually emerge within a month of the stressor and resolve within 6 months, unless the stressor persists for a longer duration

Empirical evidence for the proposed ICD-11 concept of AD has been obtained from population-based studies (Maercker et al., 2012, 2008; Zelviene et al., 2017) and in in high-risk populations such as refugees (Dobricki et al., 2010), primary care patients (Einsle et al., 2010; Maercker et al., 2007), and psychiatric outpatients (Bachem et al., 2016; Einsle et al., 2010).

However, more research is needed in order to establish the generalizability of the ICD-11 concept to further clinical settings and to patient groups with diverse cultural backgrounds if the taxonomy is to meet the needs of clinicians worldwide.

Yet four outstanding questions arise:

1. Will the proposed definition identify the same group as those currently diagnosed with AD using the ICD-10 classification?
2. Will the new concept of AD be sufficiently distinct from PTSD with symptom descriptions that emphasize the similarity of the two disorders?
3. Will ICD-11 sufficiently separate AD from normal reactions?
4. Will ICD-11 sufficiently separate AD from MDD or GAD?

We do not have the answers to the 1st, 3rd and 4th of these questions since they have not been researched. It may be speculated that applying specific criteria to potential AD patients will result in a decrease of the number of AD diagnoses. This also raises the very serious concern that those currently receiving treatment for AD will be different from those identified in the future and with differences most apparent in countries using DSM-5 rather than ICD-11. A partial answer to the second of these questions is provided by the field study which found that, using, a case-control design with vignettes based on the proposed ICD-11 definition of AD, psychiatrists were able to distinguish AD from PTSD (Keeley et al., 2016). The decision to relinquish subtypes of AD in ICD-11 gained support in a recent study using latent-profile analysis, showing that classes were distinguished by symptom severity rather than anxiety or depressive symptoms (Glaesmer et al., 2015). Regarding the third question, it is likely that individuals who suffer from preoccupation with the stressor (e.g. excessive worry, distressing thoughts and constant rumination) and failure to adapt (e.g. impaired daily functioning, sleep difficulties, loss of interest in work or social life) differ from those that experience normal, non-pathological stress when faced with an adverse life event. However, it is less clear if they differ sufficiently from MDD and GAD. In particular, preoccupations may also be present in individuals with GAD and failure to adapt symptoms are also known in depressed patients. Studies investigating border disputes of AD according to the new concept and other anxiety- and mood disorders should be an essential next step in evaluation studies.

It is clear that there are more differences than similarities between the approaches of ICD-11 and DSM-5, making comparative research difficult. While both require a stressor, both are

viewed as self-limiting and they are classified in the Trauma and Stressor Related Disorder Category there are several fundamental differences between the classifications. The ICD-11 regards AD as a full threshold disorder, DSM-5 does not; impairment in functioning and specific symptoms are required in ICD-10 while DSM-5 requires one or the other; the subtypes have been jettisoned in ICD-11 but not in DSM-5 and there are differences in the time criteria. Thus, AD in ICD-11 is a substantially different disorder from that delineated in DSM-5. Yet the DSM-5 committee considering the criteria did not feel there was enough evidence to change the current criteria while the ICD-11 committee has made major changes. It remains to be seen which is the more valid and has the best evidence base. Who should judge this? Perhaps a joint group from each of the classification committees who would consider the international need for coherence and consistency in diagnosis?

Structured Measurement of AD using ICD-11 criteria

AD, as classified in DSM-IV and 5 and ICD-10, is not included in most structured diagnostic interviews such as the Clinical Interview Schedule (Lewis et al., 1992) or Composite International diagnostic Interview (CIDI; Kessler and Üstün, 2004). The Schedule for Clinical Assessment in Neuropsychiatry (SCAN; Wing et al., 1990), Structured Clinical Interview for DSM-IV (SCID; First et al., 2002) and the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) assess AD inadequately since the diagnosis of AD is not made if criteria for other psychiatric disorders are met. Several self-report questionnaires commonly used for the assessment of PTSD, anxiety and MDD were not predictive of AD (Kirsh et al., 2004).

Taking account of the proposed new criteria for AD in ICD-11 a schedule was developed specifically to screen for AD as a full threshold disorder (Glaesmer et al., 2015). The Adjustment Disorder New Module questionnaire (ADNM), a self-report scale is based on the three symptom clusters that were initially proposed for AD – intrusions associated with involuntary reminders, avoidance behaviours and failure to adapt (with accessory symptoms such as anxiety, MDD, poor impulse control etc.). The questionnaire is available in two versions, with either 20 items (ADNM-20; Glaesmer et al., 2015) or 29 items (ADNM-29; Einsle et al., 2010). During test construction an item pool of 55 symptoms covering the areas of intrusions, failure to adapt and accessory symptoms was drawn up and rated by a group of 22 experienced clinicians in Germany. Items soring 1 or 2 on a 4-point scale were included in the long version. The item selection for the abridged version was based on previous factor analysis (Einsle et al., 2010).

To date, studies have confirmed convergent and discriminant validity compared against a number of common psychiatric measures while test-retest reliability, internal consistency, and sensitivity to symptom change during treatment are good (Bachem et al., 2016; Einsle et al., 2010). A diagnostic cut-off score identifies individuals at high risk for developing AD (Lorenz et al., 2016). Using the ADNM to assess AD, the proposed model was tested and refined in a study using latent class analysis (LCA) and confirmatory factor analysis (Glaesmer et al., 2015). The LCA found 3 latent classes reflecting to mild, moderate and severe symptoms while the factor analysis identified a single dimension, that is, without subtypes. This is reflected in the proposed criteria (panel 7). A model with two core factors, i.e. preoccupation and failure to adapt, and a second-order factor comprising additional features of AD gained further support in confirmatory factor analysis of an independent non-clinical Lithuanian sample (Zelviene et al., 2017).

However, further studies are needed to confirm the validity of the ADNM and to evaluate the similarity and differences between the old and new construct underpinning AD (panel 8). This is particularly important as DSM-5 retains the old one and if there are substantial differences between them comparative research between the classification systems will be impossible.

Panel 8. Comment 4 – ICD-10 vs ICD-11?

She is displaying the features of failure to adapt as she suffers low mood, insomnia and tearfulness. She reports avoidance, driven by financial concerns. She cannot concentrate due to her preoccupation at what has happened. She had impairment in functioning since she was off work for one week but this has improved and she has shown determination to get help in managing the debt.

If symptoms AND impairment are required the current level of impairment would not meet the threshold as it was brief. Thus she would not be diagnosed with AD in either classification.

The Diagnostic Interview for Adjustment Disorder (DIAD; Cornelius et al., 2014) is a structured interview schedule, as distinct from screening, for diagnosing AD. It consists of 29 questions that identify distressing events, the temporal relationship between stress and development of symptoms as well as level of distress and disability. It does not incorporate the concepts proposed for ICD-11. The questions are based on the DSM-IV criteria although the requirement that when the criteria for other disorders are met AD cannot be diagnosed was deleted. This instrument treats AD as a full threshold disorder. Initial items were rated by 11 experts and then administered to a representative sample of disability claimants. These first results provide support for the validity of the DIAD for diagnosing AD. Its performance in clinical studies is yet to be determined and further work on its validity and reliability is yet to be completed. Until

such time as these tools have been tested in diverse clinical settings and their validity confirmed, the trained clinician remains the gold standard for diagnosing AD.

Old and new diagnostic tools in epidemiological studies of AD

Older studies of the prevalence of AD are likely to under-estimate it due to the inadequacy of the criteria and the manner in which the standard schedules such as SCAN and SCID measure AD and should be treated with caution. There are just a few studies using the new concept of AD as proposed for ICD-11 and these have been carried out in the general population, almost exclusively in Germany or Switzerland.

The General population: The Outcome of Depression International Study (ODIN study) was one of the few general population studies to include AD in its assessments and it found a prevalence of 1% for AD in the five European countries studied using SCAN (Ayuso-Mateos et al., 2001). This uses the ICD-concept of AD. The new criteria have been tested using the ADNM (see above) in a population over 65 and was found to be 2.3% (Maercker et al., 2008). Since then the proposed criteria and the ADMN have been modified. The shortened version was used in a German study in those between the ages of 14 and 93. Taking account of whether functional impairment was absent or present, a prevalence of 1.4% or 0.9% was obtained, demonstrating that including this, as is proposed in ICD-11, raises the threshold for diagnosis (Maercker et al., 2012). Among those in living in post-conflict regions the prevalence of AD, again using the new concept, ranged from 6 to 40% (Dobricki et al., 2010).

While developing the DIAD, the prevalence of AD was 7.4% in a group of disability claimants and those with AD scored higher on distress and functional impairment measures than those without (Cornelius et al., 2014).

Primary Care: There have been no studies of the proposed new criteria in this setting. Among the more recent studies using the ICD-10 concept, the prevalence of AD among those with psychological complaints in a multisite study in France was 9.4% and among the totality of primary care attendees 1% (Semaan et al., 2001) while a different multisite study from Spain identified a prevalence of AD of 2.94% using a structured interview (Fernández et al., 2012) but with extremely low detection rates by general practitioners. Using the DSM-IV definition,

Liaison Psychiatry: There have been no prevalence studies in this setting using the new concept of AD. Historically this is the setting in which AD has been most studied. AD is diagnosed in around 12% of referrals both in the US (Strain et al., 1998) and Europe (Huyse et al., 2001). Nevertheless, the frequency with which AD is now diagnosed is declining while the diagnosis of MDD is increasing (Semaan et al., 2001). According to the authors this may not reflect a change in the prevalence of AD but derive from the inordinate focus on MDD coupled with change in the "culture of prescribing" driving changes to the "culture of diagnosis".

A meta-analysis based on 70 studies showed that in oncological and haematological settings the rates were 19.4% for AD and 16.3% for either DSM or ICD defined depressive disorder, while in palliative care, based on 24 studies, AD was the diagnosis among 15.4% in comparison to a pooled prevalence of 16.5% for either DSM or ICD-10 defined MDD (Mitchell et al., 2011). AD was almost three times as common as MDD (13.7 versus 5.1%) in acutely ill in-patients (Strain et al., 1998). In the emergency department following self-harm, a clinical diagnosis of AD was made in 31.8% of those assessed while MDD was less common at 19.5%. This pattern was reversed when a SCID diagnosis was made (Taggart et al., 2006).

Psychiatric settings: A study of intake diagnoses using DSM-IV criteria in out-patient clinics, found that AD was the most common clinical diagnosis, made in 36% of patients, as compared to just over 11% using SCID (Shear et al., 2000) while 9% of consecutive admissions to an acute public sector unit were diagnosed clinically with AD (Koran et al., 2002). A recent study established a prevalence of 11.5% among outpatients of a psychiatric clinic in an Asian sample (Yaseen, 2017).

Models of AD

The literature provides three models that understand AD as stress response syndromes, which is in line with the approaches taken by the ICD-11 and DSM-5. Horowitz (1997) proposed that AD can be located on a stress response continuum, along with other stress response syndromes such as PTSD. Four consecutive phases of stress response are postulated, starting with a first phase of realization when emotions such as fear, sadness or rage emerge and result in a desire to avoid or escape thoughts and reminders of the stress event. The second phase is characterized by denial and refusal to face the implications of the event. The third phase refers to alternating intrusions and suppression in which unbidden thoughts, images, and pangs of emotion emerge. Intrusive memories (i.e. preoccupations) develop as the stressful information is inconsistent with

existing schemata and therefore stored in active memory. The stress response process is concluded by a working-through phase that results either in adapting to the implications of what had happened or in mental disorder or personality change (figure 1). However the empirical evidence for these consecutive phases is sparse (Creamer et al., 1992).

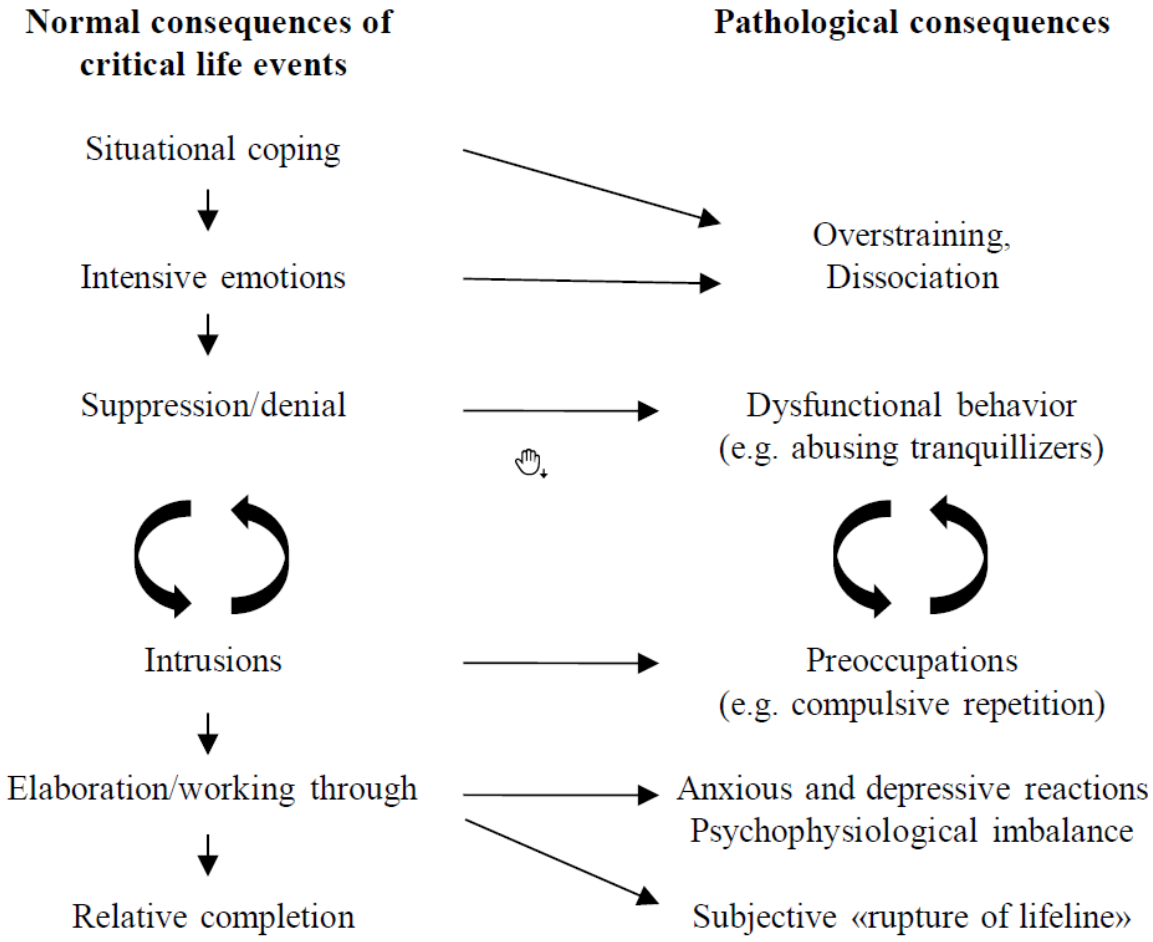

Figure 1. Model of normal and pathological stress reactions, combined from Horowitz[46] and Simmen-Janevska & Maercker[103].

Caplan's (1964) crisis model postulates typical trajectories that occur after stressful and potentially destabilizing life events. The life event is considered a problem or demand that is currently unsolvable for the individual and results in a personal crisis. Insufficient or ineffective coping mechanisms result in psychological breakdown and stress-related mental disorders. While Caplan, like Horowitz, took an essentially psychoanalytic-therapeutic perspective, Selye (1956) chose a biological approach that regards stress as a nonspecific reaction to any kind of environmental demand with symptoms increasing as the alloplastic load increases. This model highlighted the key role of the hypothalamic–pituitary–adrenocortical (HPA) axis in the human

stress response. Pathological symptoms develop when there is an imbalance of arousal and inhibitory processes with altered HPA mechanisms (Strain and Friedman, 2011) although there has been little research into the psychobiology of AD, specifically. In conclusion, the lack of empirical research on the three conceptual models applicable to AD as stress response syndrome mirrors the academic neglect regarding the symptom spectrum of AD.

Interventions

Since AD is a self-resolving condition it is unclear if treatment is required. Randomized controlled trials (RCT's) in AD of psychological and pharmacological therapies that have a slow onset of action, are hampered by the fact that these transient conditions and may have resolved spontaneously before the trial is completed. Yet AD may be protracted if the stressor continues, resulting in a substantial decline in quality of life, suicidal behavior (Kryzhanovskaya and Canterbury, 2001), and an increased suicide risk if untreated (Casey et al., 2015; Davidson et al., 1991; Gradus et al., 2010; Kryzhanovskaya and Canterbury, 2001). Furthermore, AD has been found to be a gateway disorder to more severe conditions such as MDD or anxiety disorders (O'Donnell et al., 2016). The absence of diagnostic criteria poses a problem also as this leads to difficulty identifying diagnostically homogenous subjects for trials. Potential benefits of treatment are listed in panel 9.

Panel 9. Reasons for considering treatment

To shorten duration of distressing symptoms such as sleep impairment, anxiety
To reduce chronic symptoms when the stressor is prolonged
To enhance resilience against recurring stressors
To alleviate overwhelming and disabling symptoms affecting behaviours e.g. suicidal acts
Potentially to prevent progression to depressive episode, although it is unclear if this happens

Pharmacological interventions; Evidence for the extensive use of pharmacological agents in AD, especially anti-depressants, comes from US data. Their prescription for AD showed the biggest increase from a rate of 22.26/100 to 39.37/100 annually (Olfson and Marcus, 2009). Yet there is an absence of evidence of benefit from antidepressants due to the paucity of quality RCT's and the use of pharmacotherapy is at variance with expert consensus that the treatment of choice is psychological (Strain and Friedman, 2015). Yet pragmatically if a person is not responding to psychological interventions, pharmacological treatments are used for symptom control. A

Cochrane systematic review on the pharmacological treatment of AD is currently in progress and will provide further information on the studies in this area (Casey et al., 2013).

Most double blind RCT's in AD have used herbal remedies in the anxiety subtype (ADWA). In comparison to placebo benefit has been identified for Kava kava (Volz and Kieser, 1997), valerian (Bourin et al., 1997) and ginko biloba (Woelk et al., 2007). Their mode of action is unclear. A mixed study comparing placebo, supportive psychotherapy, an antidepressant and a benzodiazepine found that all produced benefit (De Leo, 1989).

Studies examining pharmacological agents have generally been pilot studies, had small samples and no placebo arm. One found that tianeptine, alprazolam, and mianserin were equally effective at reducing symptoms in a double blind study of ADWA (Ansseau et al., 1996). In two other double blind RCT's trazodone was more effective than clorazepate in cancer patients with AD (Razavi et al., 1999) and also in HIV-positive patients with AD (De Wit et al., 1999). The best evidence is for etifoxine, a non-benzodiazepine anxiolytic, which was superior to placebo in two double blind RCT's with larger samples (Nguyen et al., 2006; Stein, 2015). But the abandonment of the subtypes as proposed in ICD-11 will further challenge pragmatic pharmacological interventions for symptom control such as anxiolytics.

Psychotherapy: Traditionally, most experts recommend integrating elements from psychosocial treatments which are established and effective for other psychiatric disorders (O'Connor and Cartwright, 2012). This presumes that the mechanisms of change from those treatments can be transferred to AD. They range from cognitive behaviour therapy (CBT), client centred psychotherapy, Gestalt psychotherapy and psychodynamic interventions to third-wave CBT techniques such as meditation. There are methodological problems with several of these studies since some are not RCT's, others have small sample sizes and some have shorter control interventions than that being tested. The studies are summarised in panel 10 (Altenhöfer et al., 2007; Ben-Itzhak et al., 2012; Cvetek, 2008; Dalgaard et al., 2014; González-Jaimes and Turnbull-Plaza, 2003; Hsiao et al., 2014; Maina et al., 2005; Srivastava et al., 2011; Van der Klink et al., 2003).

Panel 10. Overview of clinical trials evaluating AD psychological interventions

Author	Intervention	Design	*N*

Dalgaard et al. (2014)	6 sessions of CBT over 16 weeks vs two-hour workplace intervention	RCT	137
Hsiao et al. (2014)	8 weeks of body-mind-spirit group therapy vs one-session psychoeducation	RCT	17
Ben-Itzhak et al. (2012)	12 sessions of brief psychodynamic psychotherapy vs 12 months of longer-term psychodynamic psychotherapy	RCT	66
Srivastava, Talukdar, & Lahan (2011)	28 weeks of daily sessions of meditation training vs 28 sessions for 30 minutes of group counselling	RCT	30
Cvetek (2008)	3 hours EMDR vs 3 hoursactive listening vs waiting list	RCT	85
Altenhöfer, Schulz, Schwab, & Eckert (2007)	12 sessions of client-centred psychotherapy vs waiting list	Non-controlled	50
Maina, Forner, & Bogetto (2005)	Approx. 20 sessions brief dynamic therapy vs brief supportive therapy vs waiting list	RCT	30
González-Jaimes & Turnbull-Plaza (2003)	24 sessions of mirror therapy vs Gestalt psychotherapy vs medical conversation vs waiting list	Non-controlled	144
Van der Klink et al. (2003)	three month of activating intervention vs care as usual by physician	RCT	192

Disorder-specific and empirically validated psychological treatment approaches for AD are sparse but evolving. The first intervention study which considered the conceptual closeness of AD and PTSD was Eye Movement Desensitization and Reprocessing (EMDR). As seen in panel 10, this demonstrated benefit in a RCT of 90 subjects with AD (Cvetek, 2008).

One of the few disorder-specific interventions for AD is the Therapy Program for Adjustment Disorders (TAPS), a problem solving approach for individuals and groups (Reschke and Teichmann, 2008). In a pilot study, the program achieved a significant decrease in anxiety and anger symptoms, and an improvement in mood, as compared to a wait-list control group. A second intervention developed to treat AD symptoms belongs to e-mental health programs and employs a virtual reality self-help program named "EMMA's world", which is used as an addi-

tion to face-to-face treatment (Andreu-Mateu et al., 2012). The program aims to enable activation and processing of emotions and cognitions based on the theory that with repeated exposure, fear habituates. A non-controlled case series offers preliminary support for the effectiveness of the approach (Quero et al., 2017).

Low-threshold interventions characterized by high accessibility, cost-effectiveness and low barriers to treatment may be more appropriate for AD patients than longer interventions, due to their fluctuating course. These include self-help interventions, such as biblio- or online-therapy as a cost-efficient alternative to face-to-face psychotherapy. A self-help manual based on the ICD-11 conceptualisation has been evaluated in a RCT and was shown to significantly reduce symptoms of preoccupation (Bachem and Maercker, 2016). A pilot e-version of the manual is currently being evaluated in a randomized-controlled design (Maercker et al., 2015). A second web-based self-help intervention, the Brief Adjustment Disorder Intervention (BADI) is being develop by a Lithuanian team (Skruibis et al., 2016). Self-help treatments are in line with the stepped care model, and can be offered before face-to-face therapy in order to prevent the deterioration in symptoms and functioning (Williams and Martinez, 2008).

Key directions for future research

Research interest in AD has consistently increased in recent years. The publication of the ICD-11 and its explicit criteria for AD will likely stimulate much more research. In particular, it will be important to investigate the concordance of the ICD-11 and DSM-5 concepts and the effect that the diverging conceptualizations may have on diagnostic practices, prevalence rates and intervention strategies. Given the international character of the ICD-11 manual, studies evaluating the applicability and validity of the new concept in diverse cultures will be essential.

Little research has been conducted on risk and protective factors for AD. Two recent studies identified demographic risk factors of AD which included female gender, younger age, higher education, and being single (Hund et al., 2016; Yaseen, 2017). Examinations of personality, social-interpersonal factors, coping, or brain structural abnormalities have failed to identify factors that predict AD above and beyond the general risk for psychopathology such as MDD (e.g., Myung et al., 2016). In order to identify AD-specific risk factors, it has been proposed that gene-environment interactions should be investigated in future research to explain the vulnerability and resilience of individuals with regard to AD. Stress-induced alterations of the HPA axis are well known in PTSD and anxiety disorders (Jean and Groman, 2005; Morris et al., 2012; Yehuda,

2009) and it is likely that AD is also associated with altered HPA mechanisms (Strain and Friedman, 2011). These too need to be explored.

Few studies have investigated cultural issues related to AD. For example, a US-national epidemiological study has shown that Asian-American children were more likely to receive a diagnosis of AD than non-Asian children (OR = 1.66) (Nguyen et al., 2004). Furthermore, specific stressors might be relevant for certain populations such as migrants or cultural minorities (Akutsu and Abhari, 2014) while the need for developing culture-sensitive treatment methods has been stressed (Chun and Hsu, 2012). Research considering culture-specific epidemiology, aetiology and treatment is required.

An essential requirement is to resolve the border disputes on the one hand between AD and normal, adaptive reactions and on the others between AD and overlapping disorders such as depressive episode, generalised anxiety disorder and somatoform disorders. A potential starting point would be to focus on symptoms and their respective patterns using recent regression techniques such as latent class analysis. Examination of their biological underpinnings and gene-environment interactions compared to those in other overlapping disorders should also be undertaken but the results may not live up to their promise.

Given the high prevalence of AD in certain clinical settings as well as the exceptionally low rates of service use in this population (Maercker et al., 2008), effective disorder-specific interventions should be developed and evaluated. Low-threshold, non-invasive interventions such as self-help, monitoring, psychoeducation and empowerment programs may be appropriate for AD patients (Bachem and Maercker, 2016; Baumeister et al., 2009). The explicit stress response model used in ICD-11 suggests that the effectiveness of PTSD-specific interventions such as imaginary exposure or EMDR should also be investigated in the treatment of AD. However, because AD is generally self-resolving, selecting the control intervention will be important, to establish if any specific treatment is required or if general supportive measures are all that is required.

Finally, comparative studies with DSM-5 are also essential. Given the large number of individuals affected by AD and the proposals to enhance the diagnostic criteria, it is a necessary and potentially promising endeavor.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

Akutsu, P.D., Abhari, B., 2014. Adjustment disorders in Asians and Asian Americans. Asian J. Psychiatr. 7, 68–70. doi:10.1016/j.ajp.2013.12.002

Altenhöfer, A., Schulz, W., Schwab, R., Eckert, J., 2007. Psychotherapie von Anpassungsstörungen. Ist eine auf 12 Sitzungen begrenzte Gesprächspsychotherapie ausreichend wirksam? [Is psychotherapy if limited to 12 sessions sufficiently effective?]. Psychotherapeut 52, 24–34. doi:10.1007/s00278-006-0520-z

American Psychiatric Association, 2013. Diagnostic and Statistical Manual of Mental Disorders, 5th edition. American Psychiatric Association, Washington, DC.

American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th edition TR. American Psychiatric Publishing, Washington, DC.

American Psychiatric Association, 1987. Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition. American Psychiatric Association, Washington, DC.

American Psychiatric Association, 1980. Diagnostic and Statistical Manual of Mental Disorders, 2nd edition. American Psychiatric Association, Washington, DC.

American Psychiatric Association, 1952. Diagnostic and Statistical Manual of Mental Disorders, 1st edition. American Psychiatric Association, Washington, DC.

Andreu-Mateu, S., Botella, C., Quero, S., Guillén, V., Baños, R., 2012. La utilización de la realidad virtual y estrategias de psicología positiva en el tratamiento de los trastornos adaptativos [The use of virtual reality and positive psychology strategies for the treatment of adjustment disorders]. Behav. Psychol. Conduct. 20, 323–348.

Ansseau, M., Bataille, M., Briole, G., de Nayer, A., Fauchére, P.A., Ferrero, F., Mertens, C., Realini, R., Rombaut, P., Vereecken, A., Troisfontaines, B., Van Moffaert, M., 1996. Controlled comparison of tianeptine, alprazolam and mianserin in the treatment of adjustment disorders with anxiety and depression. Hum. Psychopharmacol. Clin. Exp. 11, 293–298. doi:10.1002/(SICI)1099-1077(199607)11:4<293::AID-HUP771>3.0.CO;2-Z

Arends, I., Bruinvels, D.J., Rebergen, D.S., Nieuwenhuijsen, K., Madan, I., Neumeyer-Gromen,

A., Bültmann, U., Verbeek, J.H., 2012. Interventions to facilitate return to work in adults with adjustment disorders. Cochrane database Syst. Rev. 2012, 1–115. doi:10.1002/14651858.CD006389.pub2

Ayuso-Mateos, J.L., Nuevo, R., Verdes, E., Naidoo, N., Chatterji, S., 2010. From depressive symptoms to depressive disorders: The relevance of thresholds. Br. J. Psychiatry 196, 365–371. doi:10.1192/bjp.bp.109.071191

Ayuso-Mateos, J.L., Vázquez-Barquero, J.L., Dowrick, C., Lehtinen, V., Dalgard, O.S., Casey, P., Wilkinson, C., Lasa, L., Page, H., Dunn, G., 2001. Depressive disorders in Europe: Prevalence figures from the ODIN study. Br. J. Psychiatry 179, 308–316. doi:10.1192/bjp.179.4.308

Bachem, R., Maercker, A., 2016. Self-help interventions for adjustment disorder problems: A randomized waiting-list controlled study in a sample of burglary victims. Cogn. Behav. Ther. 45, 397–413. doi:10.1080/16506073.2016.1191083

Bachem, R., Perkonigg, A., Stein, D.J., Maercker, A., 2016. Measuring the ICD-11 adjustment disorder concept: Validity and sensitivity to change of the Adjustment Disorder - New Module questionnaire in a clinical intervention study. Int. J. Methods Psychiatr. Res. 1–9. doi:10.1002/mpr.1545

Baumeister, H., Kufner, K., 2009. It is time to adjust the adjustment disorder category. Curr. Opin. Psychiatry 22, 409–412. doi:10.1097/YCO.0b013e32832cae5e

Baumeister, H., Maercker, A., Casey, P., 2009. Adjustment disorder with depressed mood. Psychopathology 42, 139–147. doi:10.1159/000207455

Ben-Itzhak, S., Bluvstein, I., Schreiber, S., Aharonov-Zaig, I., Maor, M., Lipnik, R., Bloch, M., 2012. The effectiveness of brief versus intermediate duration psychodynamic psychotherapy in the treatment of adjustment disorder. J. Contemp. Psychother. 42, 249–256. doi:10.1007/s10879-012-9208-6

Bourin, M., Bougerol, T., Guitton, B., Broutin, E., 1997. A combination of plant extracts in the treatment of outpatients with adjustment disorder with anxious mood: Controlled study versus placebo. Fundam. Clin. Pharmacol. 11, 127–132. doi:10.1111/j.1472-8206.1997.tb00179.x

Caplan, G., 1964. Principles of preventive psychiatry. Basic books, New York.

Casey, P., 2017. Personal communication.

Casey, P., 2014. Adjustment Disorder: New developments. Curr. Psychiatry Rep. 16, 1–8. doi:10.1007/s11920-014-0451-2

Casey, P., Dowrick, C., Wilkinson, G., 2001. Adjustment disorders: Fault line in the psychiatric glossary. Br. J. Psychiatry 179, 479–481. doi:10.1192/bjp.179.6.479

Casey, P., Jabbar, F., O'Leary, E., Doherty, A.M., 2015. Suicidal behaviours in adjustment disorder and depressive episode. J Affect Disord 174, 441–446. doi:10.1016/j.jad.2014.12.003

Casey, P., Maracy, M., Kelly, B.D., Lehtinen, V., Ayuso-Mateos, J.L., Dalgard, O.S., Dowrick, C., 2006. Can adjustment disorder and depressive episode be distinguished? Results from ODIN. J. Affect. Disord. 92, 291–297. doi:10.1016/j.jad.2006.01.021

Casey, P., Pillay, D., Wilson, L., Maercker, A., Rice, A., Kelly, B., 2013. Pharmacological interventions for adjustment disorders in adults (Protocol). Cochrane database Syst. Rev. 2013, 1–12. doi:10.1002/14651858.CD010530

Catalina-Romero, C., Pastrana-Jiménez, J.I., Tenas-López, M.J., Martínez-Muñoz, P., Ruiz-Moraga, M., Fernández-Labandera, C., Calvo-Bonacho, E., 2012. Long-term sickness absence due to adjustment disorder. Occup. Med. (Chic. Ill). 62, 375–378. doi:10.1093/occmed/kqs043

Chun, M., Hsu, J., 2012. Adjustment disorders in Asians, in: Chang, E.C. (Ed.), Handbook of Adult Psychopathology in Asians: Theory, Diagnosis, and Treatment. Oxford University Press, New York, NY, pp. 328–365.

Clarke, D.M., Kissane, D.W., 2002. Demoralization: Its phenomenology and importance. Aust. N. Z. J. Psychiatry 36, 733–742. doi:10.1046/j.1440-1614.2002.01086.x

Cornelius, L.R., Brouwer, S., de Boer, M.R., Groothoff, J.W., ven der Klink, J.J.L., 2014. Development and validation of the Diagnostic Interview Adjustment Disorder (DIAD). Int. J. Methods Psychiatr. Res. 23, 192–207. doi:10.1002/mpr.1418

Costello, C.G., Healy, D., 1993. Dysphoria, in: Costello, C.G. (Ed.), Symptoms of Depression. Wiley, New York, NY, pp. 24–45.

Creamer, M., Burgess, P., Pattison, P., 1992. Reaction to trauma: A cognitive processing model. J. Abnorm. Psychol. 101, 452–459. doi:10.1037/0021-843X.101.3.452

Cvetek, R., 2008. EMDR treatment of distressful experiences that fail to meet the criteria for PTSD. J. EMDR Pract. Res. 2, 2–14. doi:10.1891/1933-3196.2.1.2

Dalgaard, L., Eskildsen, A., Carstensen, O., Willert, M.V., Andersen, J.H., Glasscock, D.J., 2014. Changes in self-reported sleep and cognitive failures: A randomized controlled trial of a stress management intervention. Scand. J. Work. Environ. Health 40, 569–581. doi:10.5271/sjweh.3460

Davidson, J.R.T., Hughes, D., Blazer, D.G., George, L.K., 1991. Post-traumatic stress disorder in the community: An epidemiological study. Psychol. Med. 21, 713–721. doi:10.1017/S0033291700022352

De Leo, D., 1989. Treatment of adjustment disorders: A comparative evaluation. Psychol. Rep. 64, 51–54.

De Wit, S., Cremers, L., Hirsch, D., Zulian, C., Clumeck, N., Kormoss, N., 1999. Efficacy and safety of trazodone versus clorazepate in the treatment of HIV-positive subjects with adjustment disorders: A pilot study. J. Int. Med. Res. 27, 223–232. doi:10.1177/030006059902700502

Dobricki, M., Komproe, I.H., de Jong, J.T.V.M., Maercker, A., 2010. Adjustment disorders after severe life-events in four postconflict settings. Soc. Psychiatry Psychiatr. Epidemiol. 45, 39–46. doi:10.1007/s00127-009-0039-z

Doherty, A.M., Jabbar, F., Kelly, B.D., Casey, P., 2014. Distinguishing between adjustment disorder and depressive episode in clinical practice: The role of personality disorder. J Affect Disord 168, 78–85. doi:10.1016/j.jad.2014.06.034

Einsle, F., Köllner, V., Dannemann, S., Maercker, A., 2010. Development and validation of a self-report for the assessment of adjustment disorders. Psychol. Health Med. 15, 584–595. doi:10.1080/13548506.2010.487107

Evans, S.C., Reed, G.M., Roberts, M.C., Esparza, P., Watts, A.D., Ritchie, P.L.J., Correia, J.M., Saxena, S., 2013. Psychologists' perspectives on the diagnostic classification of mental disorders: Results from the WHO-IUpsyS Global Survey. Int. J. Psychol. 48, 177–193. doi:10.1080/00207594.2013.804189

Fabrega, H.J., Mezzich, J., 1987. Adjustment disorder and psychiatric practice: Cultural and historical aspects. Psychiatry 50, 31–49.

Fernández, A., Mendive, J.M., Salvador-Carulla, L., Rubio-Valera, M., Luciano, J. V, Pinto-Meza, A., Haro, J.M., Palao, D.J., Bellón, J.A., Serrano-Blanco, A., 2012. Adjustment disorders in primary care: Prevalence, recognition and use of services. Br. J. Psychiatry 201, 137–142. doi:10.1192/bjp.201.2.A7

First, M.B., Spitzer, R., Gibbon, M., Williams, J.B.., 2002. Structured Clinical Interview for DSM-IV-TR Axis I Disorders. New York State Psychiatric Institute, New York.

Frances, A., 1998. Problems in defining clinical significance in epidemiological studies. Arch. Gen. Psychiatry 55, 119. doi:10.1001/archpsyc.55.2.119

Friedman, M.J., Resick, P.A., Bryant, R.A., Strain, J., Horowitz, M.J., Spiegel, D., 2011. Classification of trauma and stressor-related disorders in DSM-5. Depress. Anxiety 28, 737–749. doi:0.1002/da.20845

Glaesmer, H., Romppel, M., Brähler, E., Hinz, A., Maercker, A., 2015. Adjustment disorder as proposed for ICD-11: Dimensionality and symptom differentiation. Psychiatry Res. 229, 940–948. doi:10.1016/j.psychres.2015.07.010

González-Jaimes, E.I., Turnbull-Plaza, B., 2003. Selection of psychotherapeutic treatment for adjustment disorder with depressive mood due to acute myocardial infarction. Arch. Med. Res. 34, 298–304. doi:10.1016/S0188-4409(03)00051-1

Gradus, J.L., Qin, P., Lincoln, A.K., Miller, M., Lawler, E., Lash, T.L., 2010. The association between adjustment disorder diagnosed at psychiatric treatment facilities and completed suicide. Clin. Epidemiol. 2, 23–28. doi:10.2147/CLEP.S9373

Grassi, L., Mangelli, L., Fava, G.A., Grandi, S., Ottolini, F., Porcelli, P., Rafanelli, C., Rigatelli, M., Sonino, N., 2007. Psychosomatic characterization of adjustment disorders in the medical setting: Some suggestions for DSM-V. J. Affect. Disord. 101, 251–254. doi:10.1016/j.jad.2006.11.011

Greenberg, W.M., Rosenfeld, D.N., Ortega, E.A., 1995. Adjustment disorder as an admission diagnosis. Am. J. Psychiatry 152, 459–461. doi:10.1176/ajp.152.3.459

Gutkovich, Z., Rosenthal, R.N., Galynker, I., Muran, C., Batchelder, S., Itskhoki, E., 1999. Depression and demoralization among Russian-Jewish immigrants in primary care. Psychosomatics 40, 117–125. doi:10.1016/S0033-3182(99)71257-0

Horowitz, M.J., 1997. Stress response syndromes: PTSD, grief, and adjustment disorders, ed 3. Jason Aronson, Northvale.

Hsiao, F.-H., Lai, Y.-M., Chen, Y.-T., Yang, T.-T., Liao, S.-C., Ho, R.T.H., Ng, S.-M., Chan, C.L.W., Jow, G.-M., 2014. Efficacy of psychotherapy on diurnal cortisol patterns and suicidal ideation in adjustment disorder with depressed mood. Gen. Hosp. Psychiatry 36, 214–219. doi:10.1016/j.genhosppsych.2013.10.019

Hund, B., Reuter, K., Härter, M., Brähler, E., Faller, H., Keller, M., Schulz, H., Wegscheider, K., Weis, J., Wittchen, H.-U.U., Koch, U., Friedrich, M., Mehnert, A., 2016. Stressors, symptom profile, and predictors of adjustment disorder in cancer patients. Results from an epidemiological study with the Composite International Diagnostic Interview, adaptation for oncology (CIDI-O). Depress. Anxiety 33, 153–161. doi:10.1002/da.22441

Huyse, F.J., Herzog, T., Lobo, A., Malt, U.F., Opmeer, B.C., Stein, B., De Jonge, P., Van Dijck, R., Creed, F., Crespo, M.D., Cardoso, G., Guimaraes-Lopes, R., Mayou, R., Van Moffaert, M., Rigatelli, M., Sakkas, P., Tienari, P., 2001. Consultation-Liaison psychiatric service delivery: Results from a European study. Gen. Hosp. Psychiatry 23, 124–132. doi:10.1016/S0163-8343(01)00139-6

Jablensky, A., 2016. Psychiatric classifications: Validity and utility. World Psychiatry 15, 26–31. doi:10.1002/wps.20284

Jean, K., Groman, J., 2005. The psychobiology of anxiety. Clin. Neurosci. Res. 4, 335–347. doi:10.1016/j.cnr.2005.03.008

Jones, R., Yates, W.R., Zhou, M.H., 2002. Readmission rates for adjustment disorders: Comparison with other mood disorders. J. Affect. Disord. 71, 199–203. doi:10.1016/S0165-0327(01)00390-1

Keeley, J.W., Reed, G.M., Roberts, M.C., Evans, S.C., Robles, R., Matsumoto, C., Brewin, C.R., Cloitre, M., Perkonigg, A., Rousseau, C., Gureje, O., Lovell, A.M., Sharan, P., Maercker, A., 2016. Disorders specifically associated with stress: A case-controlled field study for ICD-11 mental and behavioural disorders. Int. J. Clin. Heal. Psychol. 16, 109–127. doi:10.1016/j.ijchp.2015.09.002

Kendell, R., Jablensky, A., 2003. Distinguishing between the validity and utility of psychiatric diagnoses. Am. J. Psychiatry 160, 4–12. doi:10.1176/appi.ajp.160.1.4

Kessler, R.C., Üstün, B.B., 2004. The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int. J. Methods Psychiatr. Res. 13, 93–117. doi:10.1002/mpr.168

Kirsh, K.L., McGrew, J.H., Passik, S.D., 2004. Difficulties in screening for adjustment disorder, Part II: An attempt to develop a novel self-report screening instrument in cancer patients undergoing bone marrow transplantation. Palliat. Support. Care 2, 33–41. doi:10.1017/S1478951504040052

Koran, L.M., Sheline, Y., Imai, K., Kelsey, T.G., Freedland, K.E., Mathews, J., Moore, M., 2002.

Medical disorders among patients admitted to a public-sector psychiatric inpatient unit. Psychiatr. Serv. 53, 1623–1625. doi:10.1176/appi.ps.53.12.1623

Kryzhanovskaya, L., Canterbury, R., 2001. Suicidal behavior in patients with adjustment disorders. Cris. J. Cris. Interv. Suicide Prev. 22, 125–131. doi:10.1027//0227-5910.22.3.125

Lewis, G., Pelosi, a J., Araya, R., Dunn, G., 1992. Measuring psychiatric disorder in the community: A standardized assessment for use by lay interviewers. Psychol. Med. 22, 465–486. doi:10.1017/S0033291700030415

Lönnqvist, J.K., Henriksson, M.M., Sisometsä, E.T., Marttunen, M.J., Heikkinen, M.E., Aro, H.M., Kuoppasalmi, K.I., 1995. Mental disorders and suicide prevention. Psychiatry Clin. Neurosci. 49, 111–116. doi:10.1111/j.1440-1819.1995.tb01912.x

Lorenz, L., Bachem, R., Maercker, A., 2016. The Adjustment Disorder–New Module 20 as a screening instrument: Cluster analysis and cut-off values. Int. J. Occup. Environ. Med. 7, 215–22. doi:10.15171/ijoem.2016.775

Maercker, A., Bachem, R.C., Lorenz, L., Moser, C.T., Berger, T., 2015. Adjustment disorders are uniquely suited for eHealth interventions: Concept and case study. JMIR Ment. Heal. 2, e15. doi:10.2196/mental.4157

Maercker, A., Brewin, C.R., Bryant, R.A., Cloitre, M., Ommeren, M., Jones, L.M., Humayan, A., Kagee, A., Llosa, A.E., Rousseau, C., 2013a. Diagnosis and classification of disorders specifically associated with stress: Proposals for ICD-11. World Psychiatry 12, 198–206. doi:10.1002/wps.20057

Maercker, A., Brewin, C.R., Bryant, R.A., Cloitre, M., Reed, G.M., van Ommeren, M., Humayun, A., Jones, L.M., Kagee, A., Llosa, A.E., 2013b. Proposals for mental disorders specifically associated with stress in the International Classification of Diseases-11. Lancet 381, 1683–1685. doi:10.1016/S0140-6736(12)62191-6

Maercker, A., Einsle, F., Kollner, V., 2007. Adjustment disorders as stress response syndromes: A new diagnostic concept and its exploration in a medical sample. Psychopathology 40, 135–146. doi:10.1159/000099290

Maercker, A., Forstmeier, S., Enzler, A., Krüsi, G., Hörler, E., Maier, C., Ehlert, U., 2008. Adjustment disorders, posttraumatic stress disorder, and depressive disorders in old age: Findings from a community survey. Compr. Psychiatry 49, 113–120. doi:10.1016/j.comppsych.2007.07.002

Maercker, A., Forstmeier, S., Pielmaier, L., Spangenberg, L., Brähler, E., Glaesmer, H., 2012.

Adjustment disorders: Prevalence in a representative nationwide survey in Germany. Soc. Psychiatry Psychiatr. Epidemiol. 47, 1745–1752. doi:10.1007/s00127-012-0493-x

Maina, G., Forner, F., Bogetto, F., 2005. Randomized controlled trial comparing brief dynamic and supportive therapy with waiting list condition in minor depressive disorders. Psychother. Psychosom. 74, 43–50. doi:10.1159/000082026

Manoranjitham, S.D., Rajkumar, A.P., Thangadurai, P., Prasad, J., Jayakaran, R., Jacob, K.S., 2010. Risk factors for suicide in rural south India. Br. J. Psychiatry 196, 26–30. doi:10.1192/bjp.bp.108.063347

McHugh, P.R., Slavney, P.R., 2012. Mental illness - Comprehensive evaluation or checklist? N. Engl. J. Med. 366, 1853–1855. doi:10.1056/NEJMp1202555

Mitchell, A.J., Chan, M., Bhatti, H., Halton, M., Grassi, L., Johansen, C., Meader, N., 2011. Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: A meta-analysis of 94 interview-based studies. Lancet Oncol. 12, 160–174. doi:10.1016/S1470-2045(11)70002-X

Morris, M.C., Compas, B.E., Garber, J., 2012. Relations among posttraumatic stress disorder, comorbid major depression, and HPA function: A systematic review and meta-analysis. Clin. Psychol. Rev. 32, 301–315. doi:0.1016/j.cpr.2012.02.002

Myung, W., Na, K.-S., Ham, B.-J., Oh, S.-J., Ahn, H.-W., Jung, H.-Y., 2016. Decreased medial frontal gyrus in patients with adjustment disorder. J. Affect. Disord. 191, 36–40. doi:10.1016/j.jad.2015.11.028

Nguyen, L., Arganza, G.F., Huang, L.N., Liao, Q., Nguyen, H.T., Santiago, R., 2004. Psychiatric diagnoses and clinical characteristics of Asian American youth in children's services. J. Child Fam. Stud. 13, 483–495. doi:10.1023/B:JCFS.0000044729.93879.c2

Nguyen, N., Fakra, E., Pradel, V., Jouve, E., Alquier, C., Le Guern, M., Micallef, J., Blin, O., 2006. Efficacy of etifoxine compared to lorazepam monotherapy in the treatment of patients with adjustment disorders with anxiety: A double-blind controlled study in general practice. Hum. Psychopharmacol. Clin. Exp. 21, 139–149. doi:10.1002/hup.757

O'Connor, B.P., Cartwright, H., 2012. Adjustment Disorder, in: Sturmey, P., Hersen, M. (Eds.), Handbook of Evidence-Based Practice in Clinical Psychology. John Wiley & Sons, Hoboken, NJ, pp. 493–506.

O'Donnell, M.L., Alkemade, N., Creamer, M., McFarlane, A.C., Silove, D., Bryant, R.A., Felmingham, K., Steel, Z., Forbes, D., 2016. A longitudinal study of adjustment disorder

after trauma exposure. Am. J. Psychiatry 173, 1231–1238. doi:10.1176/appi.ajp.2016.16010071

Olfson, M., Marcus, S.C., 2009. National patterns in antidepressant medication treatment. Arch. Gen. Psychiatry 66, 848–856. doi:10.1001/archgenpsychiatry.2009.81

Parker, G., 2005. Beyond major depression. Psychol. Med. 35, 467–474. doi:10.1017/S0033291704004210

Polyakova, I., Knobler, H.Y., Ambrumova, A., Lerner, V., 1998. Characteristics of suicidal attempts in major depression versus adjustment reactions. J. Affect. Disord. 47, 159–167. doi:10.1016/S0165-0327(97)00137-7

Quero, S., Andreu-Mateu, S., Moragrega, I., Baños, R.M., Molés, M., Nebot, S., Botella, C., 2017. Un programa cognitivo-conductual que utiliza la realidad virtual para el tratamiento de los trastornos adaptativos: Una serie de casos [A cognitive-behavioral therapy program utilizing virtual reality for the treatment of adjustment disorders: A case seri. Rev. Argentina Clínica Psicológica 26, 5–18.

Razavi, D., Kormoss, N., Collard, A., Farvacques, C., Delvaux, N., 1999. Comparative study of the efficacy and safety of trazodone versus clorazepate in the treatment of adjustment disorders in cancer patients: A pilot study. J. Int. Med. Res. 27, 264–272. doi:10.1177/030006059902700602

Reed, G.M., Correia, J.M., Esparza, P., Saxena, S., Maj, M., 2011. The WPA-WHO global survey of psychiatrists' attitudes towards mental disorders classification. World Psychiatry 10, 118–131.

Reschke, K., Teichmann, K., 2008. Entwicklung und Evaluation eines kognitiv-behavioralen Therapieprogramms für Patienten mit Anpassungsstörung [Development and evaluation of a cognitive-behavioral psychotherapy program for patients with adjustment disorder]. Psychosom. und Kons. 2, 98–103. doi:10.1007/s11800-008-0099-z

Rivas Rodríguez, M., Nuevo, R., Chatterji, S., Ayuso-Mateos, J.L., 2012. Definitions and factors associated with subthreshold depressive conditions: A systematic review. BMC Psychiatry 12, 1–7. doi:10.1186/1471-244X-12-181

Runeson, B.S., Beskow, J., Waern, M., 1996. The suicidal process in suicides among young people. Acta Psychiatr. Scand. 93, 35–42. doi:10.1111/j.1600-0447.1996.tb10616.x

Selye, H., 1956. The stress of life. McGraw-Hill, New York, NY.

Semaan, W., Hergueta, T., Bloch, J., Charpak, Y., Duburcq, A., Le Guern, M.E., Alquier, C., Rouillon, F., 2001. Cross-sectional study of the prevalence of adjustment disorder with anxiety in general practice. Encephale 27, 238–244.

Semprini, F., Fava, G.A., Sonino, N., 2010. The spectrum of adjustment disorders: Too broad to be clinically helpful. CNS Spectr. 15, 382–388. doi:10.1017/S1092852900029254

Shear, M.K., Greeno, C., Kang, J., Ludewig, D., Frank, E., Swartz, H. a., Hanekamp, M., 2000. Diagnosis of nonpsychotic patients in community clinics. Am. J. Psychiatry 157, 581–587. doi:10.1176/appi.ajp.157.4.581

Sheehan, D. V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59, 22–33. doi:10.1016/S0924-9338(99)80239-9

Simmen-Janevska, K., Maercker, A., 2011. Anpassungsstörungen: Konzept, Diagnostik und Interventionsansätze [Adjustment Disorders: Model, Assessments and Interventions]. Psychother. Psychosom. Medizinische Psychol. 61, 183–192.

Skruibis, P., Eimontas, J., Dovydaitiene, M., Mazulyte, E., Zelviene, P., Kazlauskas, E., 2016. Internet-based modular program BADI for adjustment disorder: Protocol of a randomized controlled trial. BMC Psychiatry 16, 1–7. doi:10.1186/s12888-016-0980-9

Spitzer, R.L., Wakefield, J.C., 1999. DSM-IV diagnostic criterion for clinical significance: Does it help solve the false positives problem? Am. J. Psychiatry 156, 1856–1864.

Srivastava, M., Talukdar, U., Lahan, V., 2011. Meditation for the management of adjustment disorder anxiety and depression. Complement. Ther. Clin. Pract. 17, 241–245. doi:10.1016/j.ctcp.2011.04.007

Stein, D.J., 2015. Etifoxine versus alprazolam for the treatment of adjustment disorder with anxiety: A randomized controlled trial. Adv. Ther. 32, 57–68. doi:10.1007/s12325-015-0176-6

Stein, D.J., Lund, C., Nesse, R.M., 2013. Classification systems in psychiatry: Diagnosis and global mental health in the era of DSM-5 and ICD-11. Curr. Opin. Psychiatry 26, 493–497. doi:10.1097/YCO.0b013e3283642dfd

Strain, J., Friedman, M.J., 2015. Adjustment disorders, in: Gabbard, G.O. (Ed.), Gabbard's Treatments of Psychiatric Disorders (5th Ed.). American Psychiatric Publishing,

Arlington, VA, pp. 519–529.

Strain, J., Friedman, M.J., 2011. Considering adjustment disorders as stress response syndromes for DSM-5. Depress. Anxiety 28, 818–823. doi:10.1002/da.20845

Strain, J., Smith, G.C., Hammer, J.S., McKenzie, D.P., Blumenfield, M., Muskin, P., Newstadt, G., Wallack, J., Wilner, A., Schleifer, S.S., 1998. Adjustment disorder: A multisite study of its utilization and interventions in the consultation-liaison psychiatry setting. Gen. Hosp. Psychiatry 20, 139–149. doi:10.1016/S0163-8343(98)00020-6

Taggart, C., O'Grady, J., Stevenson, M., Hand, E., Mc Clelland, R., Kelly, C., 2006. Accuracy of diagnosis at routine psychiatric assessment in patients presenting to an accident and emergency department. Gen. Hosp. Psychiatry 28, 330–335. doi:10.1016/j.genhosppsych.2006.05.002

Van der Klink, J.J.L., Blonk, R.W.B., Schene, A.H., Van Dijk, F.J.H., 2003. Reducing long term sickness absence by an activating intervention in adjustment disorders: A cluster randomised controlled design. Occup. Environ. Med. 60, 429–437. doi:10.1136/oem.60.6.429

Volz, H.P., Kieser, M., 1997. Kava-kava extract WS 1490 versus placebo in anxiety disorders. A randomized placebo-controlled 25-week outpatient trial. Pharmacopsychiatry 30, 1–5. doi:10.1055/s-2007-979474

Williams, C., Martinez, R., 2008. Increasing access to CBT: Stepped care and CBT self-help models in practice. Behav. Cogn. Psychother. 36, 675–683. doi:10.1017/S1352465808004864

Wing, J.K., Babor, T., Brugha, T., Burke, J., Cooper, J.E., Giel, R., Jablenski, A., Regier, D., Sartorius, N., 1990. SCAN. Schedules for clinical assessment in neuropsychiatry. Arch. Gen. Psychiatry 47, 589–593. doi:10.1001/archpsyc.1990.01810180089012

Woelk, H., Arnoldt, K.H., Kieser, M., Hoerr, R., 2007. Ginkgo biloba special extract EGb 761 in generalized anxiety disorder and adjustment disorder with anxious mood: A randomized, double-blind, placebo-controlled trial. J. Psychiatr. Res. 41, 472–480. doi:10.1016/j.jpsychires.2006.05.004

World Health Organisation, 1978. The ninth revision of the International Classification of Diseases and Related Health Problems (ICD-9). World Health Organisation, Geneva.

World Health Organization, 1992. The ICD-10 classification of mental and behavioural disorders: Clinical description and diagnostic guidelines. World Health Organization,

Geneva.

Yaseen, Y.A., 2017. Adjustment disorder: Prevalence, sociodemographic risk factors, and its subtypes in outpatient psychiatric clinic. Asian J. Psychiatr. 28, 82–85. doi:10.1016/j.ajp.2017.03.012

Yehuda, R., 2009. Status of glucocorticoid alterations in post-traumatic stress disorder. Ann. N. Y. Acad. Sci. 1179, 56–69. doi:10.1111/j.1749-6632.2009.04979.x

Zelviene, P., Kazlauskas, E., Eimontas, J., Maercker, A., 2017. Adjustment disorder: Empirical study of a new diagnostic concept for ICD-11 in the general population in Lithuania. Eur. Psychiatry 40, 20–25. doi:10.1016/j.eurpsy.2016.06.009