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# Psychological interventions for patients with rheumatic diseases and anxiety or depression

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The prevalence of clinical anxiety and clinical depression in rheumatic diseases is about twice the prevalence seen in the general population. At a milder level, the occurrence of psychological distress that does not fulfil diagnostic criteria of anxiety and depression is even higher. Evidence indicates that this high prevalence is multifactorial. Correlational studies suggest that possible factors for anxiety and depression include the suffering accompanying somatic symptoms, functional limitations, pro-inflammatory cytokines, helplessness due to the uncontrollable, unpredictable and progressive nature of the disease, and other factors associated with having a chronic disease. This article reviews the prevalence and diagnosis of anxiety and depression in rheumatic diseases and it examines the contents and the impact of psychological interventions to address these difficulties for patients.

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Rheumatic diseases appear to increase the risk of developing anxiety and depression. Anxiety as manifested in worrying and tenseness along with avoidance behaviour may be triggered by the presence of pain and fatigue. Depression is revealed in feelings of sadness and helplessness to such an extent that it interferes with daily functioning. Several variables are potential risk factors for the development and maintenance of mood disorders in rheumatic diseases; for instance, pro-inflammatory cytokines, functional limitations, the suffering accompanying somatic symptoms and the uncontrollable and unpredictable nature of the disease. In the general population, the prevalence of anxiety and depression is higher in women than in men [1]. Since the prevalence of rheumatic diseases is also higher in women than men, there is an increased likelihood that health-care professionals in rheumatology will be relatively frequently confronted with patients needing help for anxiety or depression.

The treatment of anxiety and depression is important in its own right as treating the distress is an important issue for patients. An additional reason to treat this distress is that it affects how well people are able to manage their rheumatic disease and, thus, has an impact on their health outcomes. For instance, the anxious avoidance of physical activity may increase functional impairment, and pessimistic thoughts may lead to poor adherence to pharmacological treatment or reduced attending the physician in the event of a disease exacerbation. Both clinical and subclinical (mild) depression have been found to be independent predictors of mortality in rheumatoid arthritis [2,3]. Moreover, health-care consumption [4,5], medical costs, sick leave [6] and job loss [7] are increased among patients with rheumatic diseases suffering from high levels of psychological distress.

This article reviews the prevalence, diagnosis and psychological interventions for anxiety and depression in patients with rheumatic diseases. The criteria of the *Diagnostic and statistical manual of mental disorders* (DSM-IV) of the American Psychiatric Association [8] are used for the classification of mental disorders into distinct categories. However, only considering clinical disorders of anxiety and depression fails to capture the increased frequency of depressed and anxious mood experienced by patients with rheumatic conditions that do not reach levels to achieve a clinical diagnosis. In this article, we discuss interventions for patients with a clinical diagnosis of anxiety and depression as well as for the milder cases. Recent (past 10 years) literature was searched on Web of Science and Scopus with an emphasis on meta-analyses and systematic reviews; the search terms were 'anxiety' or 'depression' combined with any rheumatic disease.

## Anxiety

*Joanne, 34 years, is married with John. She has two daughters. Caroline is 7 years and Deborah is 5 years. Three years ago rheumatoid arthritis was diagnosed. Since that time the arthritis keeps her home. She often feels worried and anxious. She is worried that her children will be involved in a motor vehicle accident. She hides from her neighbors because she fears that they abuse her of being a malingerer. Even the smallest argument with her husband can lead to a series of catastrophic scenarios about him leaving her for another woman. When there is a problem about insurance on the television, she starts worrying about her own insurance. Actually, she is worrying all the time; even when she should be sleeping she is worrying. Although rationally Joanne knows that her worry is excessive, she is unable to control her anxiety and worries and incapable to relax and enjoy herself. The worries and preoccupation coincide with restlessness, irritability, concentration problems, and fatigue. She envies other people who appear to live their life careless, without any worries. The core problem for Joanne is that her social, occupational, and other important areas of functioning are hampered by excessive, uncontrollable anxiety and worry about a number of events or activities, occurring more days than not. Joanne possibly meets criteria for generalized anxiety disorder.*

Anxiety is a major mental health problem that is likely to confront the rheumatology health-care professional. The presentation may vary. For example, patients may have intense anxiety about physical symptoms as is characteristic of panic disorder or they may experience intense fear when they are alone in public places as in agoraphobia. In addition, features of their physical limitations and general appearance may lead to fear of being evaluated negatively by others, which is a hallmark

feature of social phobia, or they may – like Joanne – suffer excessive and uncontrollable worry about everyday issues as in generalised anxiety disorder. Although these symptoms are, obviously, not always present at clinical levels and may fail to meet criteria for a clinical diagnosis of anxiety, even subclinical levels of anxiety may pose a threat to well-being and functioning [9].

People with rheumatic disease likely experience anxiety from time to time, because uncertainty about the course and progression is an integral aspect of the disease. However, the role of anxiety in rheumatic disease has received less attention from researchers than the role of depression. This is salient because several studies have shown that anxiety is prevalent in rheumatic disease [10]. It is also important that there is generally a high level of co-morbidity between anxiety and depressive symptoms [10].

### Prevalence

In a cross-sectional study, the proportion of people with rheumatoid arthritis who scored above the 'probable clinical state' threshold for anxiety was approximately four times greater than in controls [11]. In another study, 20% of people with arthritis suffered an anxiety disorder compared with 13% of those without arthritis [12]. In a study comparing rates of anxiety and depression, it was found that 20–30% of patients with rheumatoid arthritis experienced increased levels of anxiety at different assessment points in a 10-year period, compared to 5–15% of patients experiencing elevated depression [13]. A further study showed that, compared to normative scores, people with rheumatoid arthritis, particularly those with co-morbid depression, experienced elevated trait anxiety [14]. The occurrence of anxiety appears also high in other rheumatic diseases, for example, in fibromyalgia [15] or ankylosing spondylitis [16]; however, patients with osteoarthritis did not differ from normative samples on either state or trait anxiety [14].

### Assessment and diagnosis

Several easily administrable self-report questionnaires are available to assess anxiety symptoms. Examples are listed in Table 1. Some of these screening questionnaires can be used to assess anxiety symptoms among other symptoms [17,18], while others assess anxiety alone [19,20], some guided by the diagnostic criteria for anxiety disorders as distinguished in DSM-IV [21,22]. Several frequently used questionnaires in rheumatic diseases such as the Short-Form 36 (SF-36) and the Arthritis Impact Measurement Scales (AIMS-2) use anxiety items as part of assessment of more generic constructs such as mental well-being (SF-36) and mood (AIMS-2), but these questionnaires do not provide anxiety subscales.

It is important that anxiety has a number of different forms. In DSM-IV, eight main categories of anxiety disorders are distinguished [8]. These categories and their main features are shown in Table 2. All anxiety disorders have in common that they are characterised by intense anxiety, coinciding with avoidance behaviour and physical symptoms, although the precise object of the fear, or 'key concern', differs between disorders. The case of Joanne illustrates how generalised anxiety disorder may enhance the distress of people with rheumatic diseases.

**Table 1**

Self-report questionnaires to assist in the assessment of anxiety symptoms.

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HADS, Hospital Anxiety and Depression Scale includes a 7-item anxiety subscale and a 7-item depression subscale [17].
SCL-90, Symptom Checklist includes a 10-item anxiety subscale among other dimensions of emotional symptoms [18].
STAI, State-Trait Anxiety Inventory assesses state anxiety (20 items) and trait anxiety (20 items) [19].
ASI, Anxiety Sensitivity Index measures sensitivity to the presence of anxiety, a process related to panic attacks, 16 items [20].
SPIN, Social Phobia Inventory assesses fear, avoidance, and physiological symptoms that characterize social phobia, 17 items [21].
GAD-Q-IV, Generalized Anxiety Disorder Questionnaire for DSM-IV inventories symptoms of generalized anxiety disorder according to DSM-IV [22].
DSM-IV, Diagnostic and Statistical Manual of the American Psychiatric Association [8].

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**Table 2**

Diagnosis of anxiety disorders in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [8].

	Main category	Features
1	Panic disorder (with or without agoraphobia)	Recurrent sudden episodes of intense fear based on catastrophic misinterpretations of basically benign bodily sensations.
2	Agoraphobia (with or without panic disorder)	Intense fear and avoidance of particular situations and places where it is difficult or embarrassing to escape; these are mostly public places (busy supermarkets, train stations, cinemas).
3	Specific phobia	Fear and avoidance associated with particular situations (small places, heights), animals (spiders, mice) or fear of medical procedures.
4	Social phobia	Fear of being negatively evaluated by others.
5	Obsessive compulsive disorder	Obsessive thoughts about some particular catastrophe that one is perceived as being co-responsible for, alone or in combination with compulsive behaviours that are aimed at warding off this catastrophe.
6	Posttraumatic stress-disorder	Persistent reexperiencing symptoms, avoidance, and anxiety/increased arousal following exposure to a traumatic event.
7	Acute stress disorder	Dissociative symptoms, reexperiencing symptoms, avoidance, and anxiety/increased arousal, occurring within four weeks of a traumatic event.
8	Generalised anxiety disorder	Excessive, uncontrollable worry about everyday issues that is disproportionate to the actual source of worry (issues related to, e.g., finance, health, relationships or work).

As noted, although anxiety symptoms are prevalent among people with a rheumatic disease, these are not always sufficiently severe to pass the threshold for a formal anxiety disorder as defined in DSM. State anxiety refers to an unpleasant emotional arousal in response to a perceived threat, while trait anxiety refers to stable individual differences in a predisposition to experience anxiety in anticipation of threatening situations [19]. State anxiety may be a perfectly normal response, but a high level of trait anxiety is troublesome. Anxiety and stress are related but not identical concepts [14].

### Determinants

It is important to appreciate a distinction in the type of factors predicting anxiety. Fixed factors, such as age and gender, may indicate particular groups of patients at an increased risk. Modifiable factors, in particular psychological factors, are potential treatment targets. Demographic characteristics, disease-related variables and psychological factors have been studied as predictors of self-reported anxiety.

In studies in rheumatic diseases – especially rheumatoid arthritis – female gender, a younger age and a lower income, but not education and marital status, have been identified as predictors of anxiety in some studies [23–29]. Some studies observed that anxiety may be elevated in patients with an early diagnosis, but anxiety levels have not been found to differ according to disease duration [14,23,25–27,30–32].

The notion that disease activity is a risk factor for anxiety has received little support. Anxiety has been associated with joint scores and the Disease Activity Scale-28 (DAS-28), an observational disease activity index including tender and swollen joint scores and inflammatory parameters [23,25,27]. These correlations may reflect that anxiety is related to observable features of the disease such as tender and swollen joints or the underlying disease process. However, anxiety has mostly been shown to be not associated with the erythrocyte sedimentation rate (ESR), C-reactive protein levels and rheumatoid factor positivity [23,25–27]. These lack of relations between anxiety and inflammatory parameters has been found in rheumatoid arthritis as well as in systemic lupus erythematosus [32,33] and suggests that anxiety is not associated with the underlying pathological process.

To deal with stressful situations, self-efficacy and coping are considered important. Self-efficacy is the belief that one is capable to perform competently in specific situations. Coping refers to cognitive and behavioural efforts to manage specific demands that are appraised as taxing. In rheumatoid arthritis, pain and disability have been found to be associated with anxiety [23,34]. However, when the

psychological processes of self-efficacy and coping are taken into account [35], this relationship is no longer apparent. This is important as it suggests the potential to limit the consequences of the disease by altering these processes [34]. In addition, high levels of social support, such as being cared by and having assistance available from family or friends, may protect against anxiety [25].

In a longitudinal study across a 5-year period following the diagnosis of rheumatoid arthritis, less decrease of anxiety was predicted by a lower education level, more disease activity and functional disability, and the personality characteristic neuroticism [30]. People high on neuroticism – which is strongly related to chronic anxiety – tend to avoid negative situations. Avoidance behaviour is a crucial factor in the persistence of anxiety and fear [36].

Most of the above studies involved self-report measures of anxiety symptoms. The number of patients with a clinical diagnosis of anxiety disorder was generally not identified. To treat clinical anxiety, psychotherapists will generally rely on conventional psychological interventions including cognitive-behavioural interventions targeting maladaptive cognitions and avoidance behaviour, and interventions focussed on increasing self-efficacy.

### *Treatment*

Selective serotonin reuptake inhibitors (SSRIs) generally represent the first-line pharmacological treatment approach in anxiety disorders [37]. Of the non-pharmacological therapies available, cognitive-behavioural therapy appears the preferred first-line treatment for anxiety disorders [38]. Cognitive-behavioural therapy employs a variety of techniques including cognitive restructuring, exposure and behavioural experiments [39] (Table 3). The rationale behind cognitive restructuring is that intense, persistent negative emotions (including anxiety) and maladaptive coping behaviours (e.g., avoidance or safety-seeking behaviours) do not directly result from particular situations and 'activating events', but instead follow from how these situations and events are appraised or perceived. Accordingly, one important means to alleviate emotional suffering and foster constructive coping behaviour is by (a) identifying the maladaptive cognitions that underlie a person's suffering in particular situations and circumstances, (b) examining the validity and utility of these cognitions and (c) reformulating these cognitions into cognitions that are associated with less intense suffering and facilitate rather than block constructive action. In the treatment of panic symptoms in a person with rheumatic disease, cognitive restructuring could, for instance, focus on altering catastrophic misinterpretations that particular, basically benign, bodily symptoms signal further deterioration of health or some other mental or physical catastrophe. Likewise, in a person with social anxiety, restructuring could focus on excessively negative inferences about how one appears to others.

Exposure involves step by step confrontation with avoided stimuli and a breaking down of avoidance behaviours and safety-seeking behaviours. In the aforementioned example of panic, this could involve eliciting and confronting particular physical symptoms and exposure to public places the person has learned to avoid, while refraining from cognitive or behavioural attempt to minimise these physical symptoms.

Behavioural experiments are specified actions or assignments that patients undertake to test their catastrophic misinterpretations and reduce maladaptive avoidance behaviours [40]. In the social anxiety example, someone could be encouraged to talk about his pain or limitations with another person, to test the prediction that this will lead to negative and rejecting responses. Further typical cognitive-behavioural interventions include relaxation training (which targets the physiological

**Table 3**

Cognitive-behavioural therapy.

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A main premise of cognitive-behavioural therapy is that negative, dysfunctional thoughts have a perpetuating role in health problems. Cognitive-behavioural therapy is directed at reduction of symptoms like depression, anxiety, pain, and physiological responses by changing maladaptive thoughts and behaviour. Examples are interventions with one specific aim—for example, relaxation, stress reduction or overcoming of fear-avoidance beliefs to support an exercise intervention and, more commonly, the incorporation of various methods—for example, cognitive restructuring of dysfunctional beliefs or "worry" thoughts, pain coping skills training, activity pacing, stress management training, relaxation exercises, exposure to anxious situations, thoughts and worries, and positive self-talk.

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components of the anxiety) and positive self-talk (an intervention focussed on practicing and rehearsing positive thoughts about the self).

Cognitive-behavioural therapy is the treatment of choice for anxiety symptoms and syndromes [41]. Illustrative in this regard are meta-analytic reviews which have shown that cognitive-behavioural therapy is an effective treatment for generalized anxiety disorder as compared to wait-list or treatment-as-usual control groups [42]. There is evidence that cognitive-behavioural therapy for generalized anxiety disorder is more effective than pharmacotherapy in terms of long-term maintenance of treatment effects [38].

There is growing evidence that cognitive-behavioural therapy is also effective in reducing anxiety in patients with rheumatic disease [43,44]. For instance, a recent meta-analytic review indicated that cognitive-behavioural interventions, focussed on changing negative cognitions and increasing physical activity levels, are beneficial for many patients with rheumatoid arthritis [43]. In general as well as in rheumatic diseases, cognitive-behavioural therapy typically involves some combination of cognitive restructuring, behavioural interventions (e.g., increasing physical activity and relaxation) and stress management (Table 3), and it is mostly delivered in 10–20 1-h sessions taking place weekly or once every 2 weeks by trained clinical psychologists (psychotherapists), although there is evidence that protocolised therapies can be delivered effectively by trained nurses and social workers [40].

## Depression

*Sarah, housewife, is 56 years of age. She is married to Bill, has a 24-year-old son who married lately and a 21-year-old daughter who studies abroad. For more than 20 years, Sarah suffers from systemic lupus erythematosus, but disease activity is low most of the time. She did not have prednisone during the past 12 years. Most often, Sarah came alone to the consultation, but this time her husband Bill came with her. Bill explained: "Lately, Sarah mostly just sits down on the couch. Especially in the morning, she's unable to do anything; she does not read the paper; she does nothing at all." Sarah has lost weight in the past months. She awakens very early in the morning; sometimes after having slept for only a few hours. She feels worthless and guilty about not being motivated to do the household tasks. She is glad that the children have all left home. Things would be even worse, if they would still be around...*

Sarah obviously needs a referral to a clinical psychologist or psychiatrist, who will likely conclude that she is depressed and needs treatment for her depression. Clinical depression is also known as major depressive disorder and unipolar depression [8]. Other depressive disorders are dysthymic disorder (chronic depression with less severe but longer lasting symptoms than major depressive disorder) and bipolar (manic-depressive) disorders [8]. This review mainly focusses on major depressive disorder.

## Prevalence

The prevalence of depression in rheumatoid arthritis is estimated at between 10% and 20%, approximately twice the rate seen in the general population [10,12,45,46]. When this prevalence estimate is adjusted for gender, marital status, age, income and presence of one or more health conditions other than rheumatoid arthritis, the odds ratio of depression is 1.63 [12]. Using a questionnaire assessment, 'probable' depression was reported in 20% of patients with rheumatoid arthritis, 17% of those with osteoarthritis of the hip or knee and 14% of those with osteoarthritis of the hands [47]. A longitudinal panel study examined long-term patterns of depression in rheumatoid arthritis and found that a high proportion of patients with rheumatoid arthritis was affected by chronic (9%) and intermittent levels of depression (25%) over time [46]. A systematic review with meta-analysis compared levels of depressed mood in people with rheumatoid arthritis, osteoarthritis, fibromyalgia and healthy controls [48]. The depressed mood levels of people with rheumatoid arthritis were significantly higher than the levels of healthy controls (the difference was small to moderate) and of people with osteoarthritis (the difference was very small), whereas people with fibromyalgia had higher depressed mood levels than those with rheumatoid arthritis (the difference was small).

**Table 4**

Diagnosis of clinical depression.

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The diagnosis of clinical depression according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [8] is established when a person experienced at least five of the following symptoms, most of the time almost everyday during the same 2-week period, which represent a change from the person's previous level of functioning. One of the symptoms must be either 'depressed mood' or 'loss of interest or pleasure'. The symptoms must be of a severity that interferes with normal functioning.

1. Depressed mood.
  2. Significantly reduced level of interest or pleasure.
  3. Considerable loss or gain of weight or change in appetite.
  4. Insomnia or hypersomnia.
  5. Psychomotor agitation or retardation.
  6. Fatigue or loss of energy.
  7. Feelings of worthlessness or extreme guilt (not about being ill).
  8. Reduced ability to think, concentrate or make decisions.
  9. Suicidal thoughts or suicide attempt.
- 

### Assessment and diagnosis

The diagnosis of clinical depression requires a clinical interview performed by an appropriately qualified practitioner such as a psychiatrist or clinical psychologist. Table 4 shows the diagnostic criteria of clinical depression [8].

Health-care professionals working in rheumatology must always be alert to the possibility that a patient suffers from depression. A number of screening questionnaires exist to assist in the identification of depressed mood (Table 5) [17,49–53].

To screen for depression in their regular clinical interview, health-care professionals in rheumatology can use two key questions concerning mood and interest such as recommended by the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom [54] and guidelines for general practitioners in several countries:

1. During the last month, have you often been bothered by feeling down, depressed or hopeless?
2. During the last month, have you often been bothered by having little interest or pleasure in doing things?

### Determinants

Factors predicting depression in rheumatic diseases have received more attention than those predicting anxiety. This paragraph reviews factors predicting self-reported depression above a cut-off on a questionnaire or interview-based assessments of depression as diagnosed by professionals using criteria of the Diagnostic and Statistical Manual of the American Psychiatric Association or International Classification of Diseases (ICD).

In cross-sectional studies, female gender, younger and older age, being unmarried, lower education level and lower income have been shown to be associated with depression in patients with a rheumatic disease [55–58], but these associations have frequently not been found [23,24,55–60]. The duration of the rheumatic disease does not appear to differ between patients with and without depression [32,55,59–61].

**Table 5**

Self-report questionnaires to assist in the screening of depressed mood.

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- HADS, Hospital Anxiety and Depression Scale, a 7-item anxiety subscale and a 7-item depression subscale [17].
  - HAM-D or HDRS, Hamilton Rating Scale for Depression, 17 items [49].
  - MHI-5, Mental Health Inventory, 5 items [50].
  - CES-D, Center for Epidemiologic Studies Depression Scale, 20 items [51].
  - BDI-II, Beck Depression Inventory, 21 items [52].
  - PHQ-9, Patient Health Questionnaire, 9 items [53].
-



The unfavourable consequences of the disease process for depression could be mediated by cytokines, small proteins that serve to regulate the immune system [62]. During inflammation, pro-inflammatory cytokines such as tumour necrosis factor  $\alpha$  (TNF $\alpha$ ) and interleukin-6 (IL-6) signal the brain that may induce sickness behaviour consisting of depressed mood and a constellation of other non-specific responses such as weakness, inability to concentrate and lethargy [63]. Indeed, disease activity has been associated with depression in rheumatoid arthritis both in cross-sectional [23,59,60] and in longitudinal research [23]. It has also been found in systemic lupus erythematosus [55] and in systemic sclerosis [58]. In addition, more severe pain, fatigue and disability have been related to depression, both cross-sectionally [23,46,56,57,59,60] and longitudinally [23]. With respect to psychological factors, low self-esteem and maladaptive cognitive-behavioural patterns such as fear avoidance, helplessness, catastrophising and passive pain coping strategies have been shown important in rheumatic diseases [60,64–67]. These factors may play a role not only in depression, but also in anxiety.

It is important that the finding of a correlation between disease activity variables and depression does not prove that depression is a direct consequence of disease activity. This relation may be mediated by psychological factors or another factor may be driving the relation. Depression may be an indirect consequence of psychological mechanisms such as the burden of symptoms and the uncontrollable nature of rheumatic diseases and their unpredictable course that may make patients more vulnerable to depression by mechanisms of learned helplessness. The relation between depression, disease activity and cognitive-behavioural variables is complex. The studies above gain support for the notion that a painful, disabling and, to a certain extent, uncontrollable and unpredictable illness could lead to depression. However, the relationship between these variables is not necessarily unidirectional; depression influences other outcomes in rheumatic disease such as cognitive-behavioural variables and functional abilities and it may impact on disease activity. Patients with depression are less compliant to treatment regimens [68] and fewer patients show positive effects of drug treatment [23,69].

### *Treatment*

#### *Mild depression*

Depressed mood or mild depression may occur without vegetative symptoms that are prevalent in clinical depression, such as sleep disturbance, change of appetite and low energy. Some patients with mild depression may improve while being monitored without additional help. Also guided physical exercise and guided self-help could be tried in case of mild depression.

In the United Kingdom, the following general measures are recommended in the treatment guidelines of the National Institute for Health and Clinical Excellence: (1) sleep hygiene and anxiety management, (2) watchful waiting during 2 weeks, (3) exercise and (4) cognitive-behavioural therapy guided self-help consisting of appropriate written materials and limited support from a health-care professional, who typically introduces the self-help programme and reviews the progress and outcome [54]. More structured therapies, such as problem-solving, brief cognitive-behavioural therapy consisting of only a few sessions, or counselling can be helpful. Antidepressants do not appear to be more effective than placebo in acute milder depressions or very mild major depression [70].

#### *Moderate to severe depression*

Antidepressant drugs and more extensive psychological therapies, such as longer-term cognitive-behavioural or interpersonal psychotherapy, are not recommended as an initial treatment, but these interventions may be offered when simpler methods (e.g., guided self-help or exercise) have failed to produce an adequate response.

For several decades, tricyclic antidepressants were the first-line treatment of depression. Nowadays, antidepressant drugs of choice are, in the first instance, SSRIs, such as fluoxetine, paroxetine, fluvoxamine, citalopram and sertraline [71]. No published comparative study of the newer antidepressants such as those aimed at inhibition of the reuptake of serotonin and noradrenalin (serotonin and noradrenaline reuptake inhibitors (SNRIs)) has enrolled a large enough group of patients to have the power to detect reliably differences between the new treatment and an existing effective treatment [72]. Because pro-inflammatory cytokines may promote depression, the blockade of pro-inflammatory



cytokines with biologicals such as infliximab, etanercept or adalimumab may turn out to be a new therapy for depression in rheumatoid arthritis [73].

Antidepressants are effective in the acute treatment of major depression of moderate and greater severity including major depression associated with physical illness [70,74,75]. Antidepressant medication is relatively safe and effective for many patients, but there is no evidence that they reduce the risk of recurrence once they are terminated [54].

The psychological treatment of depression will vary depending on its severity. Combined treatment involving medication and evidence-based psychotherapy typically provides a modest increment over either single treatment alone [74,76].

In both severe and mild depression, to prevent relapse or recurrence, a clinical psychologist may offer cognitive-behavioural or interpersonal psychotherapy [70,71,76]. A main premise of cognitive-behavioural therapy is that negative, dysfunctional thoughts have a perpetuating role in depression, whereas interpersonal psychotherapy is based on the premise that depression occurs in the context of interpersonal relationships. Review studies indicate long-term greater effectiveness of cognitive-behavioural therapy over tricyclic antidepressants alone [77]. Outcomes for interpersonal psychotherapy are broadly similar to the outcomes of cognitive-behavioural therapy [71,77]. Cognitive-behavioural therapy is a mainstay approach to depression [78] that has received considerable empirical support [71,79]. The capacity to reduce relapse risk after stopping pharmacological interventions is considered one of the major benefits provided by cognitive-behavioural interventions with respect to the treatment of depression, as well as for anxiety disorders [76].

### **Psychological distress in rheumatic diseases**

Studies and interventions have been done in patients with rheumatic diseases who show symptoms of depression or anxiety but do not meet the criteria for a full mood or anxiety disorder as described in DSM-IV. Psychological (or general) distress is a label that is commonly used to refer to this state. It encompasses a broad range of negative affective states such as depressed mood, sorrow, worry, irritability, apprehension, insomnia and restlessness, and is common in rheumatic diseases. According to the tripartite model of depression and anxiety [80], these symptoms are non-specific and shared by anxiety and depression disorders. Whereas conservative estimates for prevalence of a clinical mood disorder such as depression or an anxiety disorder in rheumatic diseases range from 9% to 20% [48,81], milder levels of psychological distress, as measured with self-report assessments, are more often reported, with a prevalence up to 65% in rheumatoid arthritis and osteoarthritis [60,82], ankylosing spondylitis [16] and fibromyalgia [83].

Longitudinal studies show that psychological distress predicts poor long-term outcomes [13,30,46]. A longitudinal study examined the prospective association between psychological distress and disease activity in rheumatoid arthritis patients [27]. Adjusted for baseline levels of distress, a positive association between psychological distress and disease activity was suggested when measured at the same time and when measured 6 months apart, but the results did not support the notion that psychological distress is a risk factor for future exacerbation of disease activity [27].

Psychological interventions have been developed for patients with rheumatic diseases with relatively high scores on anxiety or depressive symptoms, but who do not fulfil the DSM-IV criteria of depression or anxiety or in whom these criteria were not established. The study results suggest that over and above standard care, these psychological interventions can effectively improve physical and psychological functioning and reduce long-term health-care consumption [44,84,85]. Meta-analyses of randomised controlled trials in rheumatoid arthritis and osteoarthritis demonstrated that cognitive-behavioural therapies have been effective in improving pain, disability, coping, self-efficacy and psychological distress with small to moderate effect sizes [44,86,87]. Meta-analyses found that cognitive-behavioural therapy is moderately effective in treating depressive symptoms and depression in people with somatic diseases (effect sizes between 0.42 and 0.49) [77,88]. The magnitude of the effect size, however, was dependent on the severity of the depressive symptoms at the time of inclusion [77], suggesting that selected patients with high levels of psychological distress may benefit the most from cognitive-behavioural therapy. Also, in fibromyalgia, cognitive-behavioural therapy has been included as a treatment option [89,90]. In highly distressed patients with fibromyalgia, the

combination of cognitive-behavioural therapy and exercise training proved to be effective with respect to short- and long-term physical and psychological functioning [91].

In recent years, mindfulness-based stress reduction therapy and acceptance-based therapy have been applied in the treatment of mental problems that may accompany chronic somatic diseases (including several rheumatic diseases). These therapies add mindfulness and acceptance to traditional cognitive-behavioural techniques. Mindfulness meditation focusses on becoming aware and accepting all thoughts, feelings and sensations instead of trying to avoid or fight them. A recent randomised controlled trial examined the effects of a mindfulness-based group intervention in adults with inflammatory rheumatic diseases [92]. One out of three patients has serious psychological distress above the threshold value of 23 on the General Health Questionnaire-20. Significant better improvements in the experimental group as compared to the control group were found in psychological distress, self-efficacy, emotion-focussed coping, fatigue, self-care ability and overall well-being at post-treatment and maintained at 12 months follow-up. Recent reviews show that mindfulness-based and acceptance-based therapies have small to moderate beneficial effects on psychological distress, pain and coping that are comparable to cognitive-behavioural therapy that less specifically includes these elements [93–95].

In routine rheumatology practice, patients with impaired physical and psychosocial functioning despite adequate medical treatment pose a great challenge. Treatment outcomes may be improved by screening and selecting distressed patients based on established cut-off scores for (sub)clinical levels of anxiety and depression and offering these patients a psychological intervention such as cognitive-behavioural therapy with or without acceptance-based components.

## Discussion

This review summarised studies on the prevalence, diagnosis and psychological interventions for anxiety or depression in patients with rheumatic diseases.

The prevalence of anxiety disorders and clinical depression in rheumatic diseases was shown to be increased. Apart from patients suffering from anxiety or depression according to diagnostic criteria, a relatively large number of patients suffer from psychological distress. However, prevalence estimates differ widely, dependent on the classification criteria and assessment methods used. Moreover, symptoms of the disease such as sleep disturbances, lethargy associated with fatigue and avoidance of strenuous exercise overlap with diagnostic criteria for anxiety and depression hampering diagnoses. Finally, depressive symptoms and depression scores of patients with rheumatoid arthritis on average do not differ from other clinic patients [47]. Thus, although the prevalence of anxiety and depression is higher in rheumatic diseases than in the general population, the precise ratios are difficult to determine.

Regarding diagnosis, the criteria in the diagnostic and statistical manual of the American Psychiatric Association [8] are used to determine the presence of anxiety disorder or clinical depression. It is obvious that conventional treatment of rheumatic diseases targets the underlying disease process and primary symptoms. Attention to the psychological status and psychosocial factors that may impact on the disease is much more haphazard [96]. Paradoxically, the increased emphasis on pharmacological treatment may mask the treatment needs of some of the most severely affected by the disease [97]. Patients who were rated by their rheumatologist as having more impaired functional status were more than twice as likely to have moderately severe to severe symptoms of depression [98]. Identifying and treating anxiety and depressive symptoms is an important facet of the long-term care of patients with rheumatic diseases [99,100]. Regular mood assessment by the rheumatology clinical staff may serve to improve awareness and early identification, and thus timely identification and treatment of anxiety and depression.

Generally, studies of the determinants of anxiety and depression included the whole range of patients with rheumatic diseases. By contrast, our review of treatment of anxiety disorder and clinical depression concerned a restricted group of patients. Findings from cross-sectional and longitudinal studies in the whole range of patients do not necessarily yield the best-fitting recommendations for interventions in a specific group of rheumatic patients with co-morbid psychopathology.

In case of anxiety disorder and depression, we recommend common treatment by qualified professionals. However, the field lacks controlled evaluations of patients with rheumatic diseases who

are diagnosed with an anxiety disorder or depression according to DSM-IV criteria. Psychological interventions have been developed specifically for highly distressed patients with rheumatic diseases, but it is not known how many patients in these groups had a clinical diagnosis of anxiety or depression. Likely, treatment of anxiety and depression can best take place by qualified professionals in an interdisciplinary setting to be able to take account of specificities of the rheumatic disease and its treatment.

The diagnosis and treatment of anxiety and depression in rheumatic diseases are important not only because the distress indicates that people are suffering, but also because this psychological state may influence other outcomes such as compliance with medication and disease activity.

### Practice points

1. Screening for and monitoring of anxiety, depression and general psychological distress that impairs daily functioning beyond the limits imposed by the disease should be part of rheumatologic practice.
2. The preferred first-line psychological treatment for anxiety disorder is cognitive-behavioural therapy employing a variety of techniques including cognitive restructuring, exposure and behavioural experiments.
3. In case of mild depression, guided physical exercise and self-help guided by cognitive-behavioural therapy principles are indicated as well as watchful waiting during 2 weeks and sleep hygiene and anxiety management, if indicated.
4. In case of moderate or severe depression, more extensive psychological therapies by trained professionals are the mainstay approach to reduce relapse risk.

### Research agenda

1. To know for sure that guidelines for treatment in the general population can be used, treatment effect evaluations of psychological interventions in patients with rheumatic diseases and co-morbid anxiety disorders or clinical depression are needed.
2. It should be examined whether the conventional focus on treating the underlying disease process and primary symptoms of rheumatic diseases masks the diagnosis of anxiety and depression that need treatment.

### Summary

This article reviews the prevalence, diagnosis and psychological interventions for anxiety and depression in patients with rheumatic diseases. The prevalence of anxiety disorders and clinical depression in rheumatic diseases is about twice the prevalence seen in the general population; the prevalence of psychological distress not fulfilling diagnostic criteria of anxiety and depression is even higher. Brief questionnaires are available to screen for depression and anxiety in regular clinical practice, but diagnosis requires an interview performed by an appropriately qualified practitioner. The preferred first-line treatment for anxiety disorder is cognitive-behavioural therapy employing a variety of techniques including cognitive restructuring, exposure and behavioural experiments. In depression, when simpler methods such as guided self-help or exercise have failed to produce an adequate response, antidepressant drugs and more extensive psychological therapies are the mainstay approach to depression that has received considerable empirical support. The capacity to reduce relapse risk is considered one of the major benefits provided by cognitive-behavioural interventions with respect to the treatment of anxiety disorders and depression. In patients with rheumatic diseases and symptoms of depressive mood or anxiety without being depressed or anxious according to diagnostic criteria, cognitive-behavioural therapies have been shown effective in improving pain,

disability, coping, self-efficacy and psychological distress with small to moderate effect sizes. The treatment of anxiety and depression in rheumatic diseases is important because the distress indicates that people are suffering, but also because this psychological state may influence other outcomes such as compliance with medication and disease activity.

### Conflict of interest

None to declare.

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