Predictors of disease outcome in rheumatoid arthritis

The role of illness cognitions, coping and social support

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… scientific work ik most comparable with making a sculpture.
The process of shaping changes the details and in the long
run our thinking about the nature of the object.

Dorothee Chwilla (1996, p.152)

Contents

1

General Introduction

Rheumatoid arthritis (RA) is a systemic, inflammatory disease characterized by persistent inflammation of the joints, leading to irreversible damage. Patients suffer predominately from swollen joints, pain, and stiffness, accompanied by more general symptoms, such as fatigue and weakness, all of which may affect well-being and functioning in daily life. The course of RA fluctuates, alternating between remission and exacerbation. The fluctuating and unpredictable course of the disease leads to uncertain prognoses in individual patients. The prevalence of RA is approximately 1-2%. It affects two to three times as many women as men. Symptoms most commonly manifest in midlife, between the ages of forty and sixty. The etiology of RA is only partially known, and treatment predominantly focuses on alleviation of symptoms of inflammation and maintenance of functional status. Drug therapy is the chief mode of treatment, in addition to physical therapy, occupational therapy, surgery and patient education. In recent years, clinical practice has shifted towards more aggressive pharmacological treatment at an early stage of the disease and more integrated multidisciplinary care.

Psychological research in RA has become a topic of increasing attention in recent decades. Early attempts were directed at psychological factors, particularly personality characteristics and stressors that may affect the *onset* of the disease, without gaining much empirical support. Since the beginning of the 1980s, researchers have focused on the role of psychological factors in the *course* of RA disease outcome, including disease activity, functional disability, pain and psychological functioning. In this line of research, the consequences of RA in daily life as perceived by patients (quality of life), the way patients and significant others deal with these consequences (e.g., with coping and social support) and how these factors in turn may affect disease outcome, have received attention. At the same time, the effects of psychological interventions, particularly self-management programs and cognitive-behavioral therapy, have been examined. Although interventions have been found to be possibly beneficial for patients with RA, effects have usually been small and of short duration. The limited findings of psychological interventions were the basis of the studies conducted in this thesis (Kraaimaat et al., 1995a), which was aimed at gaining more insight into the role of psychological factors for RA disease outcome to enable the development of more goal-oriented, effective treatments.

ASSESSMENT OF DISEASE OUTCOME: HEALTH DIMENSIONS OF RA

In line with multidimensional definitions of general health and disability and RA disease outcome more specifically, at least three major dimensions of disease outcome can be distinguished in RA: disease activity, physical functioning and

psychological functioning (Meenan et al., 1980; Fries et al., 1983; Wilson & Cleary, 1995; Wolfe et al., 1999; WHO, 2001; see Figure 1).

Indicators of disease activity most directly reflect the pathophysiological process itself. To enhance comparability, core sets of disease activity measures and standardized disease activity scores have been developed (van Riel, 1992; Felson et al., 1993; Prevoo et al., 1995), consisting of at least an acute phase reactant, such as erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), and joint scores for swollen and tender joints. Physical functioning includes the main physical symptoms from which patients suffer, particularly the characteristic symptoms of pain and functional disability as well as more general symptoms of fatigue. As a result of the pathophysiological disease process and the physical symptoms, RA can have multiple effects on patient functioning, such as limitations in performing activities of daily life, dependance on others, decreased social contacts, unemployment and economic impairments (van Lankveld et al., 1993; Fex et al., 1998; van Jaarsveld et al., 1998). The extent to which patients experience limitations in daily life is reflected by the psychological functioning dimension, commonly assessed by anxiety and depressed mood.

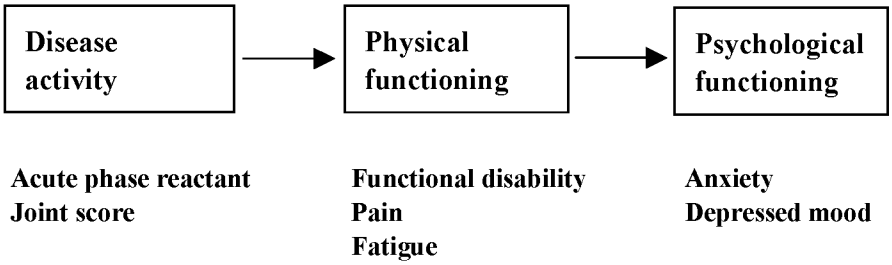

Figure 1 Indicators of disease outcome in RA

The reliable and valid assessment of RA disease outcome is a prerequisite in the study of psychological factors and the effects of therapeutic interventions. While disease activity is preferably measured by validated clinical and laboratory assessments, such as ESR or another acute phase reactant and a joint score, the dimensions of physical and psychological functioning are most frequently assessed by self-report measures. Self-report health status instruments, such as the Arthritis Impact Measurement Scales 2 (AIMS2; Meenan et al., 1992) and the Impact of Rheumatic diseases on General health and Lifestyle (IRGL; Huiskes et al., 1990a), have become complementary tools in rheumatology assessment and offer an easy, time-efficient way of gaining insight into health areas that are affected by the disease and are a focus of long-term care and therapeutic interventions.

PREDICTION OF DISEASE OUTCOME: RISK FACTORS IN RA

There is a relatively long research history focusing on the role of psychological factors in RA disease outcome. Research in this area is primarily based on two models from theoretical approaches to chronic diseases and chronic pain disorders. Stress-vulnerability models of chronic immune and autoimmune diseases and chronic diseases in general primarily attempt to predict disease activity and psychological functioning, respectively. Fear-avoidance models from the chronic pain literature can be viewed as a specification of stress-vulnerability models. In these models, the role of psychological predictors is studied with regard to a specific stressor, i.e. pain, for the prediction of primarily functional disability and pain.

In this section, the two theoretical models are introduced, followed by an overview of psychological predictors that are specified in the models. If terms for predictors in the models are used that are unfamiliar to the reader, it is possible to first read the overview of psychological predictors. The stress-vulnerability and fear-avoidance models are presented in Figures 2 and 3, respectively. Disease characteristics that may affect the role of psychological predictors in RA disease outcome will be discussed at the end of this section.

THEORETICAL MODELS

Stress-Vulnerability Models

In immune and autoimmune diseases, such as RA, the study of psychological factors and disease activity is largely based on the assumptions of stress-vulnerability models (Figure 2). Stress-vulnerability models (or diathesis-stress models or stress-coping models) for RA and other immune and autoimmune diseases propose that specific external stressors, such as major life events or disease-related stressors, and internal vulnerability factors, such as personality characteristics, can affect disease activity, due to altered functioning of the immune system (for RA, see Huyser & Parker, 1998; Walker et al., 1999). Coping with stress, social support and illness cognitions can be viewed as additional vulnerability factors that affect RA disease activity. In contrast to relatively enduring personality characteristics and irreversible stressors, it is assumed that coping, social support and illness cognitions can be changed by psychological treatments. In addition, these variables are thought to mediate the relationship of personality characteristics and stressors to disease activity, i.e. it is assumed that they at least partly account for the effects of stressors and personality characteristics on disease activity. For example, the influence of a stressful event on disease activity might be explained by how patients cope with the stressful

event. Finally, it is proposed that the different stressors and vulnerability factors affect each other. A well-known example is the buffer effect of social support on the relationship between stressors and disease activity, which means that stressors unfavorably affect disease activity only in the event of low levels of social support. In this example, social support is a moderating factor that affects the strength of the relationship between stressors and disease activity.

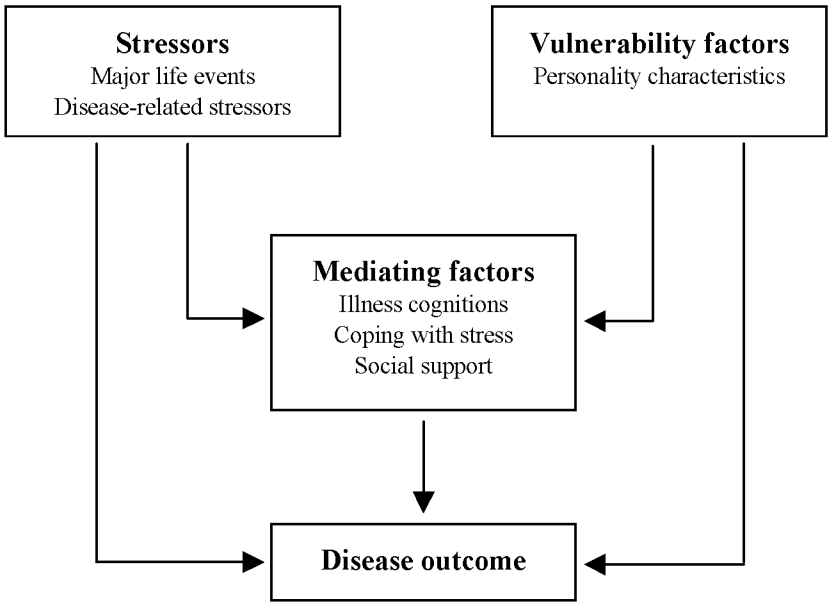

Figure 2 Stress-vulnerability models in chronic diseases

Although underlying mechanisms may differ, stress-vulnerability models aimed at predicting disease activity in immune diseases correspond to those used for predicting psychological distress in chronic diseases in general. That is, stress-vulnerability factors are assumed also to determine whether an individual develop heightened distress when faced with a chronic disease (e.g., Leventhal et al., 1984; Stanton et al., 2001). Corresponding stress-vulnerability models have also been applied for predicting physical and psychological health outcomes in the general population (e.g., Brown & Harris, 1978; Lazarus & Folkman, 1984; Steptoe, 1991a).

It should be emphasized that although stressors and vulnerability factors are viewed as distinct entities, it is not always possible to distinguish them in practice.

For example, lower levels of social support as the result of a smaller social network can be conceived both as an external stressor and an internal vulnerability factor.

Fear-Avoidance Models

In the chronic pain literature, fear-avoidance models have received considerable attention and there is supportive evidence that components of these models affect outcomes for chronic pain patients, specifically functional disability and pain (Lethem et al., 1983; Linton, 1985; Philips, 1987; see for review, e.g., Vlaeyen & Linton, 2000) (Figure 3). Fear-avoidance models propose that pain-related avoidance factors, i.e. avoidance of activity, catastrophic cognitions about pain and altered autonomic and muscular reactivity, contribute to physical deconditioning and heightened preoccupation with bodily symptoms, which in turn may enhance functional disability and pain in chronic pain patients. Social resources, such as a more extended social network and higher levels of perceived support, are assumed to stimulate social and physical activities and problem-solving capacities and beneficially affect functional disability and pain.

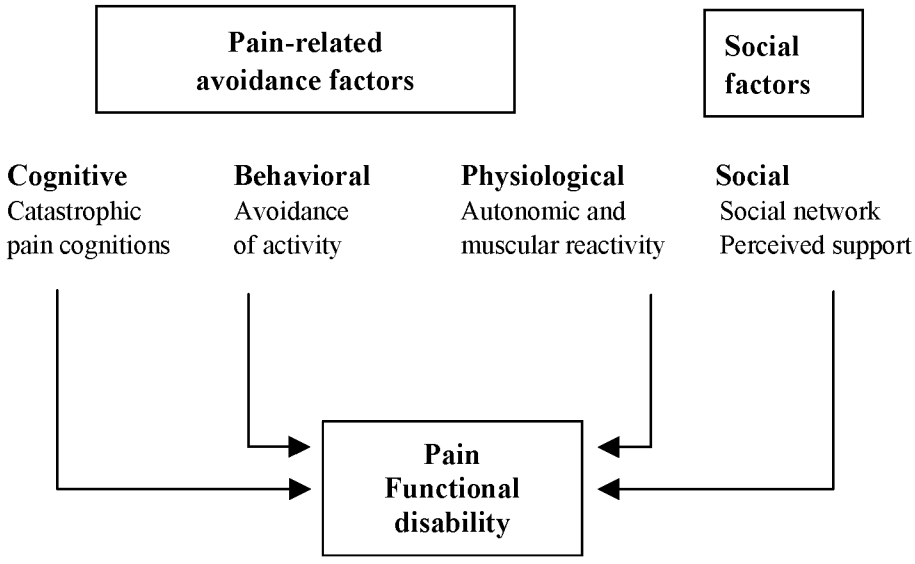

Figure 3 Fear-avoidance models in chronic pain

PSYCHOLOGICAL PREDICTORS

Based on these theoretical approaches to chronic immune diseases, chronic pain disorders, and chronic diseases in general, different psychological predictors have been studied in relationship to disease outcome in RA. Although not exclusive, main predictors can be divided into the categories of stressors, personality characteristics, coping, social support, illness cognitions, and - for chronic pain disorders - physiological pain-reactivity.

Stressors

There is a relatively long research history focusing on the role of stressors in RA disease outcome, particularly because of the supposed link between stress and RA disease activity via immunological pathways (see e.g., Anderson et al., 1984; Huyser & Parker, 1998; Walker et al., 1999). The main focus of attention has been the occurrence of major life events, assuming that these stressful events may unfavorably affect RA disease outcome. However, empirical studies linking major life events to different dimensions of RA disease outcome showed inconclusive results (e.g., Thomason et al., 1992; Koehler & Vertheim, 1993; Potter & Zautra, 1997; Dekkers et al., 2001). Less attention has been paid to the role of more long-lasting stressors that are a consequence of the disease itself, such as pain and functional disability, and the impact of the disease on daily life (cf. van Lankveld et al., 1993). Chronic, disease-related stressors can be expected to particularly affect the long-term course of disease outcome, due to their lasting impact on nearly every aspect of life (Solomon, 1981; Zautra, et al., 1989). These stressors are also expected to indirectly affect the RA disease outcome, e.g. through mediating or moderating effects of illness cognitions, coping and social support (Figure 2).

Personality Characteristics

Personality characteristics are defined as relatively stable tendencies of individuals to behave habitually across situations and over time. The most common classification of personality characteristics relates to the Big Five. Two of these five factors have been shown to be most relevant for physical and psychological health outcomes in the general population and patients with chronic diseases, including RA: neuroticism (i.e. the tendency to be relatively more tense and emotionally unstable) and extraversion (i.e. the tendency to be relatively more sociable and impulsive).

Relationships between personality characteristics, including neuroticism and extraversion, and disease activity or RA progression were repeatedly studied in early research, without gaining much support (see e.g., Moos, 1964; Anderson et al., 1984). Irrespective of the lack of relationships with biological markers, neuroticism has been linked to the report of higher levels of physical complaints in

the general population (Watson & Pennebaker, 1989; McCrae, 1990), but support for such a relationship seems to be limited in patients with RA (Affleck et al., 1992, 1994; Smith et al., 1995). Most evidently, individuals scoring high in neuroticism and, to a lesser extent, individuals scoring low in extraversion are known to experience greater psychological distress (Clark, 1994). Research in RA patients supported the role of neuroticism in future changes in psychological distress (Affleck et al., 1992). Personality characteristics are also assumed to indirectly affect the future disease outcome, as the result of mediating or moderating effects of illness cognitions, coping and social support (Figure 2).

Coping

Coping can be defined as individuals' behavioral and cognitive attempts to manage or tolerate stress (Lazarus & Folkman, 1984; Jensen et al., 1991b). Two main areas of coping research have been distinguished in RA: coping with stress in general and coping with the specific, disease-related stressor of pain (see e.g., Manne & Zautra, 1990). Stress-vulnerability models propose that an individual's reaction to stressors in general, including coping with stress, primarily affects outcomes of disease activity and psychological distress. The way individuals cope with pain, particularly cognitive and behavioral avoidance factors, is expected to play a major role in functional disability and pain, as proposed by fear-avoidance models. In both areas, the most common distinction between different categories of coping is the classification between active and passive strategies that are supposed to have favorable and unfavorable effects, respectively. In line with research on other chronic diseases and chronic pain disorders (see e.g., Jensen et al., 1991b; Stanton et al., 2001), it has repeatedly been shown that more passive-avoidant coping with stress or pain is related to worse future physical and psychological functioning in patients with RA (Felton & Revenson, 1984; Brown & Nicassio, 1987, Keefe et al., 1989; Smith & Wallston, 1992; van Lankveld et al., 1999; Scharloo et al., 1999). Much less support has been reported for the adaptive function of active coping strategies when faced with stress or pain, suggesting that not using passive coping may be more important than the use of specific active strategies for the disease outcome in RA and other chronic diseases.

Social Support

Social support can be broadly defined as interactions or resources provided by others that may help an individual cope with stress (Wills & Fegan, 2001). Although conceptualizations of social support widely differ, the most consistent distinction comprises qualitative and quantitative aspects of social support, including aspects of perceived availability of support and the size of the social network, respectively (Cohen & Wills, 1985; Wills & Fegan, 2001). Both indicators, but particularly the qualitative aspects of social support, have been shown to be related to various disease outcomes in the general population, chronic

diseases and chronic pain disorders (see for reviews e.g., Uchino et al., 1996; Wills & Fegan, 2001). As for patients with RA, there seems to be broad support for the idea that social support can affect disease outcome. For example, prospective RA studies have demonstrated that a lower level of social support is related to greater disease activity when faced with stress (Zautra et al., 1998), more interference in daily life (Smith & Wallston, 1992), more pain (Waltz et al., 1998) as well as more psychological distress (Brown et al., 1989b).

Illness Cognitions

In the literature on chronic diseases, it is commonly assumed that the way patients perceive and think about their disease accounts for much of the individual differences in their physical and psychological health status. Although conceptualizations of illness cognitions differ between models (e.g., Leventhal et al., 1984; Turk et al., 1986), there is relatively consistent evidence that specific cognitions related to the concept of control, such as helplessness, unfavorably affect the future disease outcome in RA and other chronic diseases (e.g., Smith et al., 1994; Everson et al., 1996; Parle et al., 1996; see for RA, Keefe et al., 2002). However, there are no generic self-report instruments that allow comparisons of disease-related helplessness cognitions across different chronic diseases. Far less is known about possible adaptive cognitions for individuals faced with a chronic disease, which means illness cognitions that show consistently beneficial and health-promoting effects (see Gillham & Seligman, 1999). For example, although the lack of perceived control has generally been demonstrated to be maladaptive, perceived control does not appear consistently beneficial and can adversely affect well-being in patients with RA and other chronic diseases, for example during disease flare-ups (e.g., Helgeson, 1999; Newsom et al., 1996; Schiaffino et al., 1991; Tennen et al., 1992, see also Stanton et al., 2001). It is consequently unclear whether there are generic, maladaptive and adaptive cognitions that uniformly predict disease outcome in chronic diseases, such as RA.

Physiological Pain Reactivity

Fear-avoidance models propose that not only cognitive and behavioral factors, but also physiological reactions to pain, such as enhanced autonomic and muscular reactivity, may affect pain outcomes in chronic pain patients (Figure 3). Evidence for pain-related patterns of altered autonomic and somatosensory responses has been provided for various chronic pain patients, including those with RA (e.g., Flor et al., 1985, 1992a, 1997; Jammer & Tursky, 1987; Geenen et al., 1996; see for review on RA, Anderson et al., 1985; for review on chronic pain, Flor & Turk, 1989). However, in contrast to cognitive and behavioral factors, physiological reactivity patterns in response to pain have received less attention in chronic pain literature in recent years. Support is particularly scarce for the possible maladaptive function of physiological reactivity patterns for pain outcomes. For

example, a cross-sectional study indicated that self-reported physiological reactivity to pain is related to increased pain severity in heterogeneous groups of chronic pain patients (McCracken et al., 1996), but the role of physiological pain reactivity has not yet been studied in prospective studies among RA and other chronic pain patients.

DISEASE CHARACTERISTICS

It has been repeatedly suggested that the effects of psychological predictors on RA disease outcome may depend on specific disease characteristics, such as the stage of the disease and differences between short-term and long-term outcomes.

Stage of the Disease

It has been assumed that psychological predictors are differently related to future disease outcomes at different stages of RA (Zautra et al., 1989; McFarlane & Brooks, 1990; Smith et al., 1997; Huyser & Parker, 1998). For example, psychological factors in RA have been shown to be affected by the inflammatory processes of the disease itself, its biopsychosocial consequences and pharmacological treatment with prolonged medication (van Lankveld et al., 1993; Fex et al., 1998; van Jaarsveld et al., 1998, 2000; Penninx et al., 1999, Jacobs et al., 2001), and they may be differently related to disease outcome in early and longstanding RA. However, the role of psychological predictors for future disease outcomes has usually been studied with patients with longstanding RA. By definition, early detection and modification of psychological risk factors is more likely to provide long-term benefits and to decrease an unfavorable long-term outcome of a chronic disease, such as RA. For the application of interventions at an early stage of the disease, it is important to know whether psychological predictors in early RA (e.g., at the earliest point in time - at diagnosis) affect disease outcome and whether relationships between psychological factors and disease outcome correspond to those found in patients with longstanding RA.

Duration of Effects

There is some evidence from epidemiological studies in the general population and chronic diseases that factors, such as social support, can have long-term effects on aspects like physical health and mortality (see e.g., Wills & Fegan, 2001). For patients with RA, effects of psychological factors have almost exclusively been studied for periods of approximately 1 year or less. It can be assumed that the kind of variables and the direction of effects found for short-term outcomes are not the same as for long-term outcomes over several years. For example, due to changes brought about by the disease itself or its treatment, disease-related psychological factors, such as pain coping, may have rather short-

term effects on RA disease outcome, while more general factors, such as chronic stressors and relatively stable personality characteristics, may primarily influence long-term outcomes. In addition, the strength and direction of relationships between psychological predictors and disease outcome may differ between short-term and long-term outcomes. For example, relatively generic and stable predictors, such as personality characteristics, may become evident only in the long term and factors may even work in opposite directions in different time periods, as has been found for avoidance coping (Mullen & Suls, 1982; Suls & Fletcher, 1985). To gain greater insight into the possible effects of psychological predictors on longer-term RA disease outcomes, it will be necessary to study their effects over periods of time exceeding 1 year.

MODIFICATION OF DISEASE OUTCOME: TAILORED TREATMENT IN RA

Since beginning of the 1980s, researchers have studied the effects of psychological treatments for RA patients. Interventions have usually been applied to all patients as generic group treatments. There are three main categories of interventions which differ in the degree to which changes in psychological predictors (such as coping, social support and illness cognitions) are a focus of treatment: patient education, self-management approaches and cognitive-behavioral therapy (CBT). Although interventions, particularly CBT, have been shown to be possibly effective for RA patients, recently conducted meta-analyses have indicated that psychological interventions in RA in general, and more specifically CBT and other behavioral treatments, have only marginal effects, which usually disappear at follow-up assessments (e.g., Hawley, 1995; Riemsma et al., 2002). Recent developments in RA and other chronic pain disorders suggest that customizing treatments more closely to patient characteristics in terms of patient selection and types and timing of treatment might optimize treatment effectiveness (e.g., Turk, 1990; McCracken, 1991; Devellis & Blalock, 1993; Turk & Okifuji, 1998, 2002; Gatchel, 2001), but this approach has not yet been subjected to empirical research of randomized, controlled trials in RA or other chronic pain patients.

PURPOSE OF THE STUDIES IN THIS THESIS

The studies in this thesis were conducted to gain more insight into psychological factors that affect disease outcome in RA patients. The thesis consists of three main parts, including assessment, prediction and modification of disease outcome with psychological factors and tailored treatment for RA patients. Particular attention was given to those factors that are a focus of psychological interventions, including illness cognitions, coping, and social support.

ASSESSMENT OF DISEASE OUTCOME: HEALTH DIMENIONS OF RA

Reliable and valid assessment of RA disease outcome is a prerequisite to studying the role of psychological factors and the effects of therapeutic treatments. In contrast to the clinical and laboratory assessment of disease activity, the dimensions of physical and psychological functioning are most frequently assessed by self-report health status measures. The goal of the first study *(chapter 2)* was to further validate a health status instrument for arthritis patients - the IRGL - by comparing this inventory to another widely used, international health status instrument for arthritis patients, the Dutch-AIMS2, with respect to internal consistencies, higher-order factor structures, intercorrelations, and relationships to clinical and laboratory markers in a sample of 284 RA patients.

PREDICTION OF DISEASE OUTCOME: RISK FACTORS IN RA

There is increasing evidence that psychological factors affect the RA disease outcome, especially supplied by prospective studies, in addition to a large body of cross-sectional studies and some experimental studies. Prospective studies enable the predictive value of specific factors (e.g., coping) for the future course of specific outcomes (e.g., disease activity) in a specific population (e.g., patients with RA) to be assessed. Consequently, prospective studies offer an opportunity to get an indication of possible causal relationships between the predictor and the outcome measure (in contrast to cross-sectional studies) and about the relevance and generalizability of this relationship to the population under study (in contrast to experimental research). The main part of this thesis consists of examining specific psychological predictors for the course of the RA disease outcome, using a prospective design.

The psychological predictors studied were based on two theoretical models in accordance with the psychological literature on predicting disease activity and

psychological distress in chronic (immune) diseases with stress-vulnerability models, and predicting functional disability and pain in chronic pain disorders with fear-avoidance models. Attention was given to the role of coping, social support, illness cognitions and physiological pain-reactivity. Specifically, we studied the role of coping and social support in disease outcome (disease activity, functional disability and pain, psychological distress) after 1, 3 and 5 years in a sample of recently diagnosed patients *(chapters 3.1.1 - 3.1.3).* There is preliminary evidence that coping and social support affect short-term outcomes of approximately 1 year in patients with longstanding RA. Of particular interest was whether coping and social support assessed very early in the disease process, i.e. at the time of diagnosis, would predict short-term changes in RA after 1 year as well as more long-term changes after 3 and 5 years. In addition to these studies conducted among recently diagnosed patients, the role of psychological predictors, not previously assessed in the RA literature, was studied for disease outcome after 1 year in longstanding RA patients. disease-generic illness cognitions and physiological pain reactivity *(chapters 3.2 and 3.3).*

Coping and Social Support

Predictors of disease activity. There is some theoretical and empirical support for a role of psychological factors in disease activity in autoimmune and immune diseases, such as RA. Although the role of mediating immunological changes is still unclear, research in the last decade has supplied preliminary support that psychological factors may affect RA disease activity. However, previous studies did not study the relative contribution of different stressors and vulnerability factors, including coping with stress and social support. In addition, these factors have not been studied in recently diagnosed patients and rarely for periods longer than 1 year. In the present study *(chapter 3.1.1)*, different stressors (major life events and disease-related stressors) and vulnerability factors (personality characteristics, stress coping and social support) at the time of diagnosis were studied to predict the course of clinical measures of disease activity after 1, 3 and 5 years in 78 RA patients.

Predictors of functional disability and pain. Fear-avoidance models assume that pain-related avoidance factors and social resources affect disease outcome in chronic pain patients, specifically functional disability and pain. There is some support for these models from experimental research with chronic pain patients. Prospective research has provided preliminary evidence that these factors may also be relevant to patients with longstanding RA. However, the role of these factors had not yet been assessed in recently diagnosed patients or for outcomes exceeding 1 year. In the present studies, cognitive-behavioral avoidance factors and social resources were assessed on the basis of passive pain coping strategies and social support. Specifically, the role of cognitive and behavioral pain coping and social support at the time of diagnosis was studied to predict pain and functional

disability in 91 RA patients after 1 year as well as in 78 RA patients for whom data was available after 3 and 5 years *(chapters 3.1.2.1 - 3.1.2.2).*

Predictors of psychological distress. Stress-vulnerability models attempt to explain whether patients develop psychological distress when faced with a chronic disease. Prospective studies with RA patients have shown that stress-vulnerability factors, particularly coping with stress and social support, can predict psychological distress within a period of approximately 1 year. However, previous studies have only incidentally studied the relative contribution of divergent stressors and vulnerability factors. In addition, the predictive value of stress-vulnerability factors has not been assessed in recently diagnosed patients or for periods longer than 1 year. In the present studies, different stressors (major life events, disease-related stressors) and vulnerability factors (personality characteristics of neuroticism and extraversion, stress coping and social support) at the time of diagnosis were studied to predict the course of psychological distress (anxiety and depressed mood) in 91 recently diagnosed patients after 1 year and in 78 patients for whom follow-up assessments were available after 3 and 5 years *(chapters 3.1.3.1 - 3.1.3.2).*

Illness Cognitions

The chronic diseases literature has provided promising evidence for the predictive value of illness cognitions for future disease outcomes. Illness cognitions of perceived helplessness have especially been demonstrated to have relatively uniform, maladaptive effects on disease outcomes in various chronic diseases, including RA. Far less is known about possible adaptive cognitions when individuals are faced with uncontrollable, long-term stress, such as a chronic disease. In addition, there are no generic self-report instruments that allow comparisons of maladaptive and adaptive illness cognitions across different chronic diseases. Based on the theoretical and empirical literature, it was supposed that cognitions demonstrating uniform, maladaptive and adaptive effects in chronic diseases should reflect different ways of evaluating the inherently negative meaning of a chronic disease, as indicated by cognitions of helplessness, acceptance and perceived benefits. A self-report instrument was developed to assess these illness cognitions in different chronic diseases, including RA *(chapter 3.2).* Psychometric characteristics of the instrument (reliability and concurrent and predictive validity) were studied in the total sample and randomly selected subsamples of 263 RA patients and 167 multiple sclerosis (MS) patients. Of specific interest was whether the illness cognitions would relatively uniformly predict the future disease outcome in RA and MS patients after 1 year.

Physiological Pain Reactivity

Fear-avoidance models propose that not only cognitive and behavioral factors, but also physiological reactions to pain may affect pain outcomes in chronic pain

patients. In contrast to cognitive and behavioral factors, physiological reactivity patterns to pain have received less attention in chronic pain literature in recent years. Support is particularly scarce for the possible maladaptive function of physiological reactivity patterns for pain outcomes. In addition, the role of physiological pain reactivity has not yet been examined in prospective studies among chronic pain or RA patients. In the present study, the contribution of self reported physiological pain reactivity in comparison with cognitive and behavioral avoidance factors (passive pain coping) was studied for the capacity to predict the course of pain after 1 year in a sample of 95 RA patients *(chapter 3.3).*

MODIFICATION OF DISEASE OUTCOME:
TAILORED TREATMENT IN RA

Customizing treatments more closely to patient characteristics, in terms of patient selection and types and timing of treatment, has been suggested as a way to optimize treatment effectiveness in RA and other chronic pain disorders. Based on the main findings from the present prospective studies, it was hypothesized that the effectiveness of psychological interventions for RA patients might be improved if tailor-made interventions were offered to patients at risk at a relatively early stage of the disease. Consequently, an intervention study explored whether tailored treatment to patients at risk with relatively early RA is a promising way to optimize treatment effectiveness *(chapter 4).* A randomized, controlled trial with tailor-made treatment modules was conducted with 64 patients with relatively early RA, who had been screened for psychosocial risk profiles. All patients received standard medical care from a rheumatologist and rheumatology nurse consultant. Half of the patients also received an individual, tailored cognitive-behavioral treatment (CBT). It was expected that the CBT condition would demonstrate beneficial effects on indicators of disease outcome at post-treatment and at the 6-month follow-up in comparison to the control condition.

2

Assessment of Disease Outcome

Health Dimensions of RA

A comparison of two recently developed health status instruments for patients with arthritis: Dutch-AIMS2 and IRGL

Evers, A.W.M., Taal, E., Kraaimaat, F.W., Jacobs, J.W.G., Abdel-Nasser, A., Rasker, J.J. & Bijlsma, J.W.J. (1998). A comparison of two recently developed health status instruments for patients with arthritis: Dutch-AIMS2 and IRGL. *British Journal of Rheumatology, 37,* 157-164.

ABSTRACT

Two multidimensional health status instruments of rheumatic diseases, the Dutch-AIMS2 and the IRGL, were compared in a sample of 284 rheumatoid arthritis patients with regard to their measurement properties and usefulness for research purposes. Both questionnaires showed an excellent reliability (Cronbach's α), and were highly comparable with regard to their construct and convergent validity. Second-order factor analysis confirmed the physical, psychological and social health dimensions for both questionnaires. The comparability between the instruments was established by high intercorrelations between the physical and psychological health dimensions. Sufficient convergent validity was indicated by the strong correlations between the physical functioning scales and clinical and laboratory measures. The main differences between both questionnaires relate to their length and emphasis on health aspects. The Dutch-AIMS2 is characterised by a more extensive assessment of the physical dimension and the additional measurement of general health aspects. The shorter IRGL exclusively assesses the main health dimensions with a more comprehensive measurement of the psychological and social dimensions. The instrument that reflects the subject in question most adequately should be chosen.

INTRODUCTION

Outcome assessment of rheumatic diseases is increasingly characterised by multidimensional approaches to assess the health status of patients which is, in accordance with the World Health Organisation (WHO, 1958), defined as physical, psychological and social well-being. Assessing these health dimensions requires other instruments than the sole use of clinical and laboratory data, and has resulted in the development of different self-report health status instruments. The conceptual and practical usefulness of self-report data has, for example, been demonstrated for the outcome assessment of natural history and treatment effects in rheumatoid arthritis (RA), the prediction of mortality or the utilisation and demand for health care services (Wolfe et al., 1988, 1991; Pincus et al., 1989; Bijlsma et al., 1991; Mason et al., 1992; Jacobs et al., 1993; Pincus, 1995).

In recent decades, various multidimensional health status instruments have been developed, translated and validated for the Dutch RA population: the Arthritis Impact Measurement Scales (AIMS; Meenan et al., 1980; Taal et al., 1989), the Sickness Impact Profile (SIP; Bergner et al., 1981; de Witte et al., 1987), and the Health Assessment Questionnaire (HAQ; Fries et al., 1980; Siegert et al., 1984; Bijlsma et al., 1990). Of these instruments, the AIMS most comprehensively reflected the physical, psychological and social health dimensions (Taal et al., 1989; Jacobs et al., 1992), but it was at that time also characterised by a number of psychometric problems (Huiskes et al., 1990a; Meenan et al., 1992). For these reasons, a new instrument that was derived from the AIMS was empirically developed for the Dutch arthritis population to assess the physical, psychological and social aspects of health status in a more sophisticated way: the IRGL (Impact of Rheumatic diseases on General health and Lifestyle; Huiskes et al., 1990a,b). Recently, a revised and strengthened version of the AIMS, the AIMS2, was developed and translated for application in the Dutch population of RA patients (Meenan et al., 1992; Riemsma et al, 1996). Both questionnaires, the IRGL and the Dutch-AIMS2, have proved to be reliable and valid instruments (Huiskes et al., 1990a,b; Riemsma et al., 1996) and are widely used in the Dutch arthritis population.

When selecting an instrument for use in clinical practice and research, its suitability depends on the assessment of intended health constructs, the measurement efficiency and its user friendliness. In order to facilitate the making of a decision regarding an outcome measure and to allow direct comparisons of RA samples in which one of the questionnaires was used, the Dutch-AIMS2 and the IRGL were compared with regard to their psychometric properties and usefulness for different research purposes.

METHODS

Procedure

Three hundred and thirty-seven consecutive outpatients from three hospitals in widely separated parts of the Netherlands were asked by their rheumatologists to participate in this study. Questionnaires were administered during a routine visit when clinical and laboratory data were also collected. Inclusion criteria were a minimum age of 20 years, and a diagnosis of RA assessed by a rheumatologist according to the 1987 American College of Rheumatology (ACR) criteria (Arnett et al., 1988). Correctly completed questionnaires were returned by 284 patients (85%).

Measures

Self-report data. Patients completed the two questionnaires: the Dutch-AIMS2 (Riemsma et al., 1996) and the IRGL (Huiskes et al., 1990a,b). In order to control order effects, a cross-balanced procedure was applied (for a further description of the questionnaires see the Results; for a detailed description of the AIMS2 see Meenan et al., 1992; for the IRGL see Huiskes et al., 1990a,b). In addition, the sex, age, social status, level of education, income, disease duration of patients, and use of medication were recorded.

Clinical and laboratory data. Prior to administering the questionnaires, the following disease measures were obtained: ARA functional classes (Steinbrocker et al., 1949), erythrocyte sedimentation rate (ESR), absence or presence of rheumatoid factor and bone erosions. From a subsample of 80 consecutive patients from one hospital, additional data were available on joint scores (Ritchie score; Ritchie et al., 1968), grip strength and radiographics according to the classification of Steinbrocker (Steinbrocker et al., 1949).

Statistical Analysis

Only those scales were used in the analyses which allowed comparisons between the two questionnaires, that is the physical, psychological and social functioning scales, and the disease impact scales. The two questionnaires were analysed as follows.

(1) Reliability was assessed by determining the internal consistency (Cronbach's α) (Nunnally & Bernstein, 1994) and the stability of the scales (test-retest-reliability). Test-retest reliability was assessed by determining internal consistency as well as Pearson's product moment correlation coefficients between two measurement points within a subsample of 67 consecutive patients from one hospital who completed the Dutch-AIMS2 twice with a time interval of one month.

(2) Construct validity was explored by conducting a principal component factor analysis with varimax rotation.

(3) Comparability of the instruments was assessed by computing Pearson's product moment correlation coefficients between the corresponding scales of both questionnaires.
(4) Convergent validity was assessed by computing Pearson's product moment correlation coefficients with clinical and laboratory measures, disease duration and demographic variables (age, education, income).

Normal distribution of the self-report, clinical and laboratory data was determined by skewness and kurtosis cut-offs of < 0.1 and by viewing the normal probability plots. In the case of skewness (Depressed mood scale of the IRGL, Self-care scale of the Dutch-AIMS2 and grip strength), square root transformation was applied which resulted in normal distributions of the skewed variables. All statistical analyses were carried out with the SPSS 6.1/Windows statistical package.

RESULTS

Sample

The sample was predominantly female (70%) and married or living with a partner (68%). Of the subjects, 25% had primary and 60% had secondary education. The mean age was 60 years (SD 14.5). Mean disease duration was 15.1 years (SD 11.2). The majority of the patients were classified according to functional class II or III (class I: 4%, class II: 64%, class III: 29%, class IV: 3%). The rheumatoid factor was positive in 75% and erosions were established in 76% of the patients. The mean ESR was 29.4 (SD 19.9). Most of the patients used non-steroidal anti-inflammatory drug (NSAID) and/or disease-modifying anti-rheumatic drug (DMARD) medication (80% and 81%, respectively); only a minority had oral corticosteroids or paracetamol (27% and 23%, respectively). Patients who did not return the questionnaires did not differ significantly from respondents with respect to sex, age, social status, disease duration, clinical status (ARA-class, ESR, the absence or presence of the rheumatoid factor and erosions) or the use of medication. The patients of the two subsamples who were selected for the purpose of convergent validity (n=80) and test-retest reliability (n=67) did also not differ from the main sample with respect to these characteristics.

Descriptive Comparison of the Dutch-AIMS2 and the IRGL

Questionnaires were compared with regard to their content and construction, use of response categories and time interval, scoring and the length of the questionnaires.

Content and construction. The instruments differ with respect to their method of construction and emphasis on different health aspects. The Dutch-AIMS2 was

Table 1 Health Status Scores and Internal Consistency (Cronbach's α) of the Dutch-AIMS2 and the IRGL Scales [a]

Dutch-AIMS2 Scales (number of items)	M	SD	α	IRGL Scales (number of items)	M	SD	α
Physical functioning							
Mobility (5)	2.68	2.22	0.82	Mobility (7)	17.31	6.52	0.93
Walking and bending (5)	5.46	2.56	0.80				
Hand and finger function (5)	3.64	2.53	0.89	Self-care (8)	22.60	6.61	0.94
Arm function (5)	2.59	2.47	0.88				
Self-care (4)	1.54	2.19	0.85				
Household tasks (4)	2.93	3.04	0.88				
Pain (6)	5.18	2.29	0.86	Pain (6)	15.58	4.75	0.89
Psychological functioning							
Level of tension (5)	3.89	1.97	0.88	Anxiety (10)	18.64	5.65	0.92
Mood (5)	2.86	1.55	0.80	Depressed mood (6)	3.42	3.65	0.92
				Cheerful mood (6)	11.42	4.22	0.93
Social functioning							
Support (4)	3.25	2.55	0.90	Perceived support (5)	15.77	3.80	0.94
Social activities (4)	5.08	1.16	0.65	Actual support (3)	6.69	1.81	0.68
				Mutual visit (2)	5.80	1.37	0.72
				Social network [b]			
				Neighbours (1)	2.27	0.85	
				Friends (1)	2.10	0.77	
Disease impact							
Satisfaction (12)	3.93	2.16	0.91	Disease impact (10)	21.79	6.62	0.91
Work (4)	4.39	2.70	0.77	Impact activities (5)	12.73	4.34	0.88
Arthtritis impact (1)	4.95	2.04					

[a] Theoretical scale range. Dutch-AIMS2: for all scales 0-10. IRGL: mobility 7-28; self-care 8-32; pain 6-25; anxiety and disease impact 10-40; depressed and cheerful mood 0-20; perceived support and impact activities 5-20; mutual visit 2-8; actual support 3-12;social network 1-4.

[b] Scores are categorized in norm classes (Huiskes et al., 1990a)

designed a priori and focuses more on the assessment of physical aspects than on psychological and social aspects. The aim of the empirically developed IRGL was to measure the different health dimensions in an equal constraint. Consequently, the psychological and social functioning scales are assessed more comprehensively (see Table 1 for number of scales and number of items for each health dimension). The health dimensions are assessed by the two questionnaires as follows.

(1) Physical functioning. The Dutch-AIMS2 measures the physical dimension through six functional status scales (Mobility, Walking and Bending, Hand and Finger Function, Arm Function, Self-care, Household Tasks) and one Pain scale. The IRGL dimension of physical functioning is an abridged adaptation from the Dutch-AIMS and consists of three scales (Mobility, Self-care and Pain). The functional status is measured by assessing the use of upper and lower extremities (Self-care and Mobility, respectively).

(2) Psychological functioning. Two new scales of negative affect were added in the Dutch-AIMS2 to measure psychological functioning: Mood and Level of Tension. The IRGL assesses the psychological dimension somewhat more comprehensively as positive and negative affect by three already existing scales (Anxiety, Depressed Mood and Cheerful Mood), of which the reliability and validity have been studied in the Dutch population (van der Ploeg et al., 1980; Zwart & Spooren, 1982).

(3) Social functioning. Corresponding to the broad conceptualization and operationalization of social well-being in other research areas, the social health aspects are measured differently in both questionnaires. In the Dutch-AIMS2, two new designed scales refer to the quality of social functioning: Social Activities and Support from Family and Friends. The IRGL distinguishes between qualitative and quantitative aspects of social functioning in accordance to the conceptualization of Cohen and Wills (1985). The qualitative aspect in the IRGL is measured by three scales of a Dutch validated social support scale (van Dam-Baggen & Kraaimaat, 1992): Perceived Support, Actual Support and Mutual Visits. The quantitative aspect is assessed by the size of the social network (number of friends and the number of neighbours with who one associates).

(4) Disease impact. Both questionnaires contain scales which assess the impact the disease has on the patient's life. For the Dutch-AIMS2, that is the Satisfaction scale which establishes the patient's satisfaction with 12 health areas, and the Work scale which measures the ability of the patients to carry out work (if they still work). The Arthritis Impact scale of the Dutch-AIMS2 measures the evaluation of their own health status in comparison to others and may be less comparable to the impact scales of the IRGL. The IRGL assesses the impact of the disease with one Disease Impact scale that measures the general impact of RA on several domains of daily life (e.g. work, activities, leisure, relationships, sexuality, food, sleep). The scale can be divided into four subscales of which only the Impact on Activities scale is applied for the purpose of this study.

Response category and time interval. The questionnaires differ in the application of response categories for the three health dimensions: the Dutch-AIMS2 predominantly uses two kinds of 5-point scales (always/every day - usually/most days - sometimes/some days - rarely/never); the IRGL mainly uses one kind of 4-point scale (almost never – sometimes – often - almost always). A further aspect concerns the use of time intervals. Most questions of the Dutch-AIMS2 refer to the patient's functioning within the last month, whereas time intervals in the IRGL are taken from the original scales: the physical functioning scales refer to the previous month, the psychological scales to the previous week (depressed and cheerful mood) and previous month (anxiety), and the social functioning scales to the previous half year.

Scoring. In the Dutch-AIMS2, item responses are adjusted to a 0-10 range, with 0 representing a good health status and 10 representing a poor health status (e.g. higher values of pain, mobility, and hand and finger function indicate a poor health status). By calculating the average mean, an overall physical, psychological and social interaction scale can be produced. In the IRGL, scales differ in their ranges (see Table 1) and are scored in the original direction (e.g. higher values on pain, and lower values on mobility and self-care indicate a poor health status).

Length of the questionnaires. The Dutch-AIMS2 is a more extensive questionnaire than the IRGL, mainly because of the assessment of additional health aspects, such as patients' priority areas for improvement, attribution of health problems, perception of current and future health, and a number of medical aspects (co-morbidity, medication usage, type of rheumatic disease, disease duration). The Dutch-AIMS2 consists of 71 questions with 112 single items. It takes about 20 minutes to complete. The IRGL focuses exclusively on the aforementioned health dimensions and consists of 16 questions with 68 single items. It takes about 15 minutes to complete.

User friendliness. Both questionnaires are self-administered and can be completed without (professional) assistance. As far as is known, there are no major comprehension problems with the questionnaires. In addition, the response rate was high (85%) and almost all questions were answered by the respondents.

Reliability

As demonstrated in Table 1, the internal consistency of the scales of both questionnaires is highly satisfactory. The alpha coefficients in most cases exceed 0.80 for the Dutch-AIMS2 and 0.90 for the IRGL, which indicates sufficient reliability for clinical use and patient selection, respectively (Nunnally & Bernstein, 1994). Even the somewhat lower alphas of the Social Activities and Work scales of the Dutch-AIMS2 (0.65 and 0.77, respectively), as well as the Actual Support and Mutual Visit scales of the IRGL (0.68 and 0.72, respectively), exceed the threshold value of 0.60, which indicates sufficient reliability for research purposes (Nunnally & Bernstein, 1994).

In order to assess the test-retest reliability of the Dutch-AIMS2, Cronbach's α as well as Pearson's product moment correlations between the two assessment points with a time interval of one month were calculated in the subgroup of 67 patients. Results of internal consistencies (between 0.86 and 0.96) and Pearson's product moment correlations (between 0.73 and 0.92) revealed a high test-retest reliability for the physical, psychological and social health dimensions of the Dutch-AIMS2. The strength of the alpha coefficients was similar to those previously established for the physical and psychological dimensions of the IRGL (Geenen et al., 1995).

Table 2 Factor Analysis of the Dutch-AIMS2 and the IRGL[a]

	Factor 1: Physical	Factor 2: Psychological	Factor 3: Social
Dutch-AIMS2			
Mobility	**.80**	.18	-.18
Walking and bending	**.80**	.17	-.10
Hand and finger function	**.78**	.11	-.07
Arm function	**.80**	.08	-.03
Self-care	**.78**	.13	-.05
Household tasks	**.85**	.09	-.06
Pain	**.68**	.40	.00
IRGL			
Mobility	**-.80**	-.10	.17
Self-care	**-.83**	-.16	.07
Pain	**.64**	.36	-.03
Dutch-AIMS2			
Level of tension	.20	**.74**	-.17
Mood	.38	**.73**	-.17
IRGL			
Anxiety	.19	**.84**	-.21
Depressed mood	.21	**.84**	-.10
Cheerful mood	-.14	**-.75**	.24
Dutch-AIMS2			
Support	.07	.28	**-.56**
Social activities	.27	.00	**-.69**
IRGL			
Perceived support	-.02	-.31	**.59**
Actual support	.08	-.05	**.67**
Mutual visit	-.18	-.22	**.72**
Social network			
Neighbours	-.16	.07	**.62**
Friends	.08	-.24	**.49**

[a] Loadings above 0.45 are printed in bold.

Table 3 Pearson Correlation Coefficients between the Dutch-AIMS2 and the IRGL Scales[a]

Physical functioning	IRGL		
Dutch-AIMS2	Mobility	Self-care	Pain
Mobility	**-.74**	-.65	.46
Walking & bending	**-.76**	-.54	.51
Hand & finger function	-.56	**-.78**	.43
Arm function	-.52	**-.70**	.52
Self-care	-.57	**-.65**	.42
Household tasks	**-.69**	**-.70**	.43
Pain	-.53	-.54	**.82**

Psychological functioning	Anxiety	Depressed mood	Cheerful mood
Level of tension	**.67**	**.63**	-.45
Mood	**.64**	**.67**	-.52

Social functioning	Perceived support	Actual support	Mutual visit	Social network	
				Neighbours	Friends
Support	**.48**	.24	.35	.25	.26
Social activities	.23	**.41**	**.45**	.35	.22

Disease impact	Disease impact	Impact activities
Satisfaction	**.65**	**.60**
Work	**.66**	**.63**
Arthritis impact	.45	.40

[a] All correlations significant at $p < 0.001$. Associations between similar scales are printed in bold.

Construct Validity

In order to determine the construct validity of the health dimensions, a principal component factor analysis with varimax rotation was conducted. The Disease Impact scales were excluded from this analysis, because we assumed that they would be related to all health dimensions. The criterion for factor extraction was the scree-test (Cattell, 1966) which resulted in a three-factor solution. As demonstrated in Table 2, the intended constructs of physical, psychological and social functioning were strongly supported in both questionnaires (loadings above 0.45 are printed bold). In particular, the high loadings of the physical and

psychological functioning scales (around 0.80) confirmed the assessment of clearly distinguishable dimensions. Only the pain scale of both questionnaires also loaded modestly on the psychological factor (0.40 and 0.36, respectively), reflecting the multidimensional nature of pain (Brown, 1990). The moderate loadings of the social functioning factor (between 0.49 and 0.72) indicate the more heterogeneous assessment of this construct. In total, the three-factor solution explains 61% of the total variance.

Comparability between the Dutch-AIMS2 and IRGL

Comparability was assessed by calculating bivariate correlations between the corresponding scales of the two questionnaires. As demonstrated in Table 3, the correlations between the corresponding scales (printed in bold) were high for the physical and psychological dimensions and disease impact scales (all exceeding 0.60) and indicate the measurement of rather identical constructs (see the Note). The weaker relationship between the social functioning scales again demonstrates the somewhat different assessment of this dimension. Both scales of the Dutch-AIMS2 were moderately related to the comparable qualitative scales of the IRGL (between 0.41 and 0.48), but only weakly related to the quantitative scales of the IRGL (between 0.22 and 0.35).

Convergent Validity

Correlations with demographic variables and disease duration. As physical health in rheumatic diseases has partly been shown to be related to disease duration, age and socioeconomic status (Wolfe et al., 1988; Pincus et al., 1989; Hakala et al., 1994), these correlations were also calculated for the two questionnaires. Correlations of health aspects with demographic variables (age, education and income level) and with disease duration correspond greatly in the two questionnaires (because of the large sample size, only correlation coefficients of $p < 0.001$ are mentioned). The physical functioning scales of both questionnaires were all related to age (between |0.22| and |0.30|) and disease duration (between |0.22| and |0.37|), indicating a worse functioning with older age and longer disease duration, with the exception of the relationship between age and the pain scales of both questionnaires. The impact scales of both questionnaires were also related to disease duration (between |0.24| and |0.30|), indicating a greater impact with longer disease duration. In addition, functional status scales of both questionnaires (Mobility and Hand and Finger Function of the Dutch-AIMS2 and Self-care of the IRGL) were related to income and educational level (between |0.22| and |0.24|), indicating a worse functioning for a lower socio-economic status. As expected, no substantial correlations (above $r = 0.21$) were found with the sex or the social status of the patients. In addition, none of the psychological and social functioning scales of both questionnaires were substantially related to demographic variables or disease duration.

Table 4 Pearson Correlation Coefficients between Clinical and Laboratory Measures and the Physical Functioning Scales of the Dutch-AIMS2 and the IRGL[a]

	Functional class (n = 284)	Grip strength (n = 80)	Ritchie Score (n = 80)	Radio-graphics (n = 80)	ESR (n = 284)
Dutch-AIMS2					
Mobility	.51	-.54	.40	.34	.37
Walking and bending	.50	-.30	.47	.27	.32
Hand and finger function	.50	-.67	.41	.46	.28
Arm function	.50	-.57	.36	.32	.26
Self-care	.48	-.54	.35	.28	.26
Household tasks	.61	-.55	.44	.33	.30
Pain	.40	-.29	.50		.22
IRGL					
Mobility	-.55	.54	-.54	-.30	-.41
Self-care	-.52	.67	-.36	-.49	-.25
Pain	.37	-.30	.57		.23

[a] All correlations significant.
If $n = 284$: $p < 0.001$. If $n = 80$: $r > 0.22$, $p < 0.05$; $r > 0.30$, $p < 0.01$; $r > 0.37$, $p < 0.001$.

Correlations with clinical and laboratory data. The correlation coefficients between clinical and laboratory measures (ESR, Ritchie score, grip strength, functional ARA class and radiographic score) and the physical functioning scales were significant for all scales of both questionnaires, with the expected exception of the correlation between pain and the radiographic score (see Table 4). The strength of the correlations was almost the same for the questionnaires. The physical functioning scales were strongly related to functional class and grip strength, (between |0.27| and |0.67|, in most cases exceeding |0.50|) and moderately related to the Ritchie score (between |0.35| and |0.57|; in most cases exceeding |0.40|). The weaker correlations were with radiographics (between |0.27| and |0.49|; in most cases exceeding |0.30|) and ESR (between |0.20| and |0.41|; always exceeding |0.20|), probably reflecting current disease activity rather than the patient's health status.

Note. In order to facilitate comparisons between studies in which one of the two instruments has been used, regression formulae between the most comparable physical and psychological functioning scales of the questionnaires were computed that permit the estimation of scale scores from the Dutch-AIMS2 into the IRGL: Walking and bending = -0.30 x Mobility + 10.63; Hand and finger function = -0.30 x Self-care + 10.41; Pain = 0.39 x Pain - 0.93; Level of tension = 0.23 x Anxiety - 0.41; Mood = 0.29 x Depressed mood + 1.88.

DISCUSSION

Self-report measures offer an easy and inexpensive possibility to gain insight into the patient's perceived health status and quality of life which is not offered by clinical and laboratory data. The advantages of disease-specific, multidimensional instruments compared to generic instruments or single-dimensional quality of life-measures consist of the detailed and specific information about health areas which are affected by the disease and which may change through therapeutic interventions. The comprehensive assessment of health aspects can serve as an important complementary tool in outcome assessment, therapeutic interventions, and long-term care (Wolfe et al., 1988, 1991; Pincus et al., 1989; Bijlsma et al., 1991; Mason et al., 1992; Jacobs et al., 1993; Pincus, 1995).

For the evaluation and selection of an appropriate instrument, several criteria, such as the measurement of essential health areas, user friendliness, and high reliability and validity standards of an instrument may function as a necessary guide. The results of this study indicate that both instruments, the Dutch-AIMS2 and the IRGL, meet the needs and criteria of a sophisticated and comprehensive multidimensional health instrument. In addition, both instruments provide similar, but slightly different indicators of health.

In line with previous findings (Huiskes et al., 1990a,b; Riemsma et al., 1996), reliability in terms of internal consistency is highly satisfactory for both instruments. The somewhat higher alpha of the IRGL may be due to the larger numbers of items within most scales as well as the empirical development of this questionnaire in contrast to the a priori development of the Dutch-AIMS2. In addition, a high test-retest reliability is indicated by our data for the Dutch-AIMS2, as it has been previously demonstrated for the physical and psychological scales of the IRGL (Geenen et al., 1995).

The construct validity of the Dutch-AIMS2 and the IRGL is confirmed by the results of the second-order factor analysis. The assessment of the three discrete components of health status, i.e. the physical, psychological and social functioning, is strongly supported for both questionnaires. Similar satisfactory results have also been demonstrated in previous studies for the Dutch-AIMS2 (Riemsma et al., 1996) and the IRGL (Huiskes et al., 1990a,b).

Comparability and similarity between the questionnaires were supported by strong intercorrelations within the physical and psychological health dimensions and disease impact scales, and to a lesser extent within the social functioning scales. Whereas the social scales of the Dutch-AIMS2 emphasize the extent and possibility of participating in social activities and receiving support from family and friends, the social scales of the IRGL reflect the size of the social network as well as the extent and possibility of the exchanged support.

Convergent validity was highly satisfactory and nearly identical for both questionnaires. The modest correlations of both instruments with demographic

variables, indicating a greater dysfunctioning with older age, a longer disease duration and a lower socioeconomic status, had been previously reported for the IRGL (Huiskes et al., 1990a,b) and for other health instruments (Wolfe et al., 1988; Pincus et al, 1989; Hakala et al., 1994). In addition, the strong correlations between the clinical and laboratory data and the physical functioning scales were similar to previous findings of the Dutch-AIMS2 (Riemsma et al., 1996), the IRGL (Bijlsma et al., 1991; Huiskes et al., 1990a,b; van der Heide et al., 1994) as well as other validated self-report questionnaires (Pincus et al., 1989; Mason et al., 1992; Hakala et al., 1994). Results indicate that the scales of both questionnaires assess the intended construct of physical functioning, and may serve as complementary information to clinical and laboratory data. Convergent validity of the psychological and social scales, which was not assessed in this study, had been previously established for the Dutch-AIMS2 (Riemsma et al., 1996) and for the IRGL (van der Ploeg et al., 1980; Zwart & Spooren, 1980; Kraaimaat et al., 1995b; Evers et al., 1997).

For the valid assessment of outcome research, sensitivity to change forms an essential part of the evaluation of an outcome measure. A sufficient sensitivity to change in order to detect clinically meaningful alterations after total hip replacement in osteoarthritis (OA) and RA patients has been shown in previous research for the IRGL (Borstlap et al., 1994). For the Dutch-AIMS2, studies are being undertaken to assess its sensitivity to change.

Results suggest that both questionnaires are almost identical in their high methodological standards. Differences between the instruments relate rather to their content and focus on different health aspects. The Dutch-AIMS2 measures the physical health dimension more extensively by the broader assessment of activities of daily living, and assesses additional health aspects that are not included in the IRGL, such as patients' evaluation of their health status in comparison to others, patients' priority areas for improvement, attribution of health problems, perception of current and future health, and a number of medical aspects (co-morbidity, medication usage, type of rheumatic disease, disease duration). The IRGL measures the psychological and social dimensions more comprehensively. For example, the assessment of positive affect in the psychological health dimension, which has shown to be independent of and distinctive from negative affect in previous research (Zautra et al., 1995), lacks an equivalent scale in the Dutch-AIMS2. Quantitative aspects of the social health dimension, such as the size of the social network, which is a major accompanying component of a chronic disease with ongoing disability (Evers et al., 1997), are also not represented in the Dutch-AIMS2.

The selection of an instrument must be guided by a clear definition of which health aspects are most important to assess. Depending on the research purposes and practical needs of health care providers, both questionnaires may be useful in a different way with regard to the field of interest. The focus of the Dutch-AIMS2 on

the physical functioning dimension with the extensive assessment of activities of daily living may, for example, be preferred for evaluation of physiotherapeutic interventions or surgical procedures. As an internationally applied instrument, the Dutch-AIMS2 may also be more suitable for cross-cultural research purposes. The comprehensive assessment of psychological and social aspects, as is the case in the IRGL, may be recommended in the detection of beneficial or deleterious side-effects of therapeutic interventions, or the multidisciplinary planning and decision-making of long-term care.

The brevity of an instrument and its user friendliness function as an additional selection criterion in the routine assessment of the patient's health status. For the clinical practice, the IRGL, with its exclusive focus on the main health dimensions, may be preferred because it takes less time to complete, whereas the uniform scale ranges of the Dutch-AIMS2 facilitate interpretation of the data.

The results of this study facilitate direct comparisons between two widely used multidimensional health instruments, the Dutch-AIMS2 and the IRGL, in order to make a decision regarding an appropriate outcome measure. The instruments are similar in their high reliability and validity standards, but differ slightly in their focus on different health aspects. Both can be used optimally as complementary evaluations of clinical outcome, therapeutic interventions and long-term care. The instrument that reflects the subject in question most adequately should be chosen.

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3

Prediction of Disease Outcome

Risk Factors in RA

3

3.1 Coping and Social Support

3.1.1 Predictors of disease activity

Stress-vulnerability factors as long-term predictors of disease activity in early rheumatoid arthritis

Evers, A.W.M., Kraaimaat, F.W., Geenen, R., Jacobs, J.W.G. & Bijlsma, J.W.J. (2003). Stress-vulnerability factors as long-term predictors of disease activity in early rheumatoid arthritis. *Journal of Psychosomatic Research (in press).*

ABSTRACT

Stress-vulnerability factors were studied for their ability to predict long-term disease activity in early rheumatoid arthritis (RA). In a prospective study involving 78 recently diagnosed rheumatoid arthritis patients, the role of personality characteristics (neuroticism, extraversion), physical and psychological stressors (chronic, disease-related stressors of functional disability, pain, disease impact on daily life, as well as major life events), coping and social support at the time of diagnosis was examined to predict changes in clinical indicators of disease activity 1, 3 and 5 years later. While stress-vulnerability factors failed to predict disease activity at the 1-year follow-up, disease activity at the 3 and 5-year follow-ups was predicted by coping and social support at the time of diagnosis, after adjusting for disease activity at first assessment, other biomedical and psychosocial factors and use of medication. Low levels of social support predicted increased disease activity at the 3-year follow-up, and high avoidance coping predicted increased disease activity at the 3 and 5-year follow-ups. Findings indicate the potential prognostic value of avoidance coping and social support for the long-term course of disease activity in early RA and suggest that the effects of these vulnerability factors predominantly operate in the long term.

INTRODUCTION

In recent decades, the role of stressors and stress modulating factors has been repeatedly proposed in chronic inflammatory diseases, such as rheumatoid arthritis (RA) (Anderson et al., 1985; Koehler, 1985; Huyser & Parker, 1998; Walker et al., 1999). In line with stress-vulnerability models (Steptoe, 1991a, 1998; Walker et al., 1999), various stressors and stress modulating factors have been suggested to affect the course of RA disease activity, which is only modestly predicted by biomedical factors (van der Heijde et al., 1988). However, empirical findings are far from conclusive concerning the essential factors and the direction of their effects on disease activity. Comprehensive study of the extent to which different stressors and vulnerability factors contribute to the course of disease activity may provide a more integrated understanding of psychosocial factors that affect disease activity in RA.

Most attention in RA stress research has focused on the occurrence of stressful events, particularly major life events, which are assumed to precede and increase an unfavorable course of RA. Although relationships between the occurrence of major events at onset and unfavorable disease outcomes have occasionally been reported (Latman & Walls, 1996; Leymarie et al., 1997), other studies have indicated inconclusive results (Koehler & Vertheim 1993; Potter & Zautra, 1997), and a relationship to major events could hardly be supported when clinical indicators of disease activity were applied (Thomason et al., 1992; Leymarie et al., 1997; Dekkers et al., 2001). Aside from major stressful events, minor daily stressors have been supposed to primarily affect short-term disease fluctuations in RA, but research findings have also been inconsistent (Affleck et al., 1997; Potter & Zautra, 1997; Zautra et al., 1997). Little attention has been directed to the role of more long-lasting stressors that are a direct consequence of the disease itself, such as pain and functional disability, and the impact of the disease on daily life, e.g. limited possibilities in terms of work and daily activities and changes in social relationships (van Lankveld et al., 1993; Evers et al., 1997). Due to their lasting impact on nearly every aspect of life, chronic, disease-related stressors could particularly affect the long-term course of the disease, resulting in a vicious circle of increased inflammation and chronic stress (Solomon, 1981; Zautra et al., 1989).

Aside from environmental stressors, individual and social vulnerability factors, such as personality characteristics, social support and the manner of coping with stress, have been assumed to have direct, mediating or moderating effects on RA disease activity. While personality characteristics were originally assumed to directly enhance vulnerability to the onset of RA, without gaining much support (Moos, 1964; Anderson et al., 1985), their impact on the course of disease activity has been less extensively studied. So far, the results of relationships to clinical indicators of disease activity or progression are inconclusive (Crown et al., 1975; Gardiner, 1980; Latman & Walls, 1996). Studies on physical and psychological

health outcomes rather support a mediating or modifying role for specific personality characteristics, such as neuroticism and extraversion, on exposure and reactivity to stressors (Costa & McCrae, 1987; Watson & Pennebaker, 1989; McCrae, 1990; Affleck et al., 1992, 1997; Phillips & Gatchel, 2000). The role of social support in predicting health outcomes has been widely accepted (Broadhead et al., 1983; Kaplan & Toshima, 1990; Uchino et al., 1996), and favorable direct or buffer effects of quantitative and qualitative aspects of social support, such as the size of the social network or the availability of perceived support, have been demonstrated in prospective studies for physical and psychological symptoms in RA (Brown et al., 1989b; Evers et al., 1997, 1998a). Regarding disease activity, a social support buffer effect has been suggested by the finding that the quality of spousal support moderates changes in immunological parameters in periods of interpersonal stress (Zautra et al., 1998). Another possible source of vulnerability is the coping responses individuals use when faced with stress. Based on the general distinction between active, problem-focused coping and passive avoidance coping, research has repeatedly demonstrated that the use of more passive coping, and incidentally also the use of less active coping, prospectively predicts physical and psychological symptoms in RA (Brown & Nicassio, 1987; Evers et al., 1998a; Scharloo et al., 1999). In addition, there is preliminary evidence from prospective studies for harmful effects of passive avoidance coping on RA disease activity after three years (McFarlane et al., 1987) and on self-reported disease flare-ups after one year (Brown & Nicassio, 1987). Due to the generally modest relationships found for these psychosocial factors, biomedical variables have also been posited as having a moderating effect on the stress-vulnerability relationship to disease activity. Specifically, patients without a rheumatoid factor have been reported to be more vulnerable to the stress-illness relationship (Crown et al., 1975; Gardiner, 1980; Stewart et al., 1994).

So far, empirical evidence supports a link between stressors and vulnerability factors and the course of disease activity in RA. However, definite conclusions about the specific kind of variables affecting disease activity and their relative contributions cannot be drawn from present research, since a comprehensive test of various stressors and vulnerability factors that enables the investigation of direct, mediating or modifying effects on disease activity has rarely been conducted (cf. Dekkers et al., 2001). In addition, inconclusive results found in the literature may be ascribed to differences between studies in outcomes measures, time periods assessed and stages of the disease. For example, a wide range of outcome measures has been used and researchers do not always distinguish between indicators of disease activity, such as inflammatory activity and swelling of joints, and indicators of disease outcome, such as functional disability (McFarlane et al., 1987; McFarlane & Brooks, 1990). However, disease activity and disease outcome measures may be differently modulated by psychosocial factors (Leymarie et al., 1997). In addition, the kind of variables and the direction of effects recently found

for short-term disease fluctuations (Affleck et al., 1997; Zautra et al., 1997) may be irrelevant to long-term outcomes (McFarlane & Brooks, 1990; Affleck et al., 1997). In contrast to short-term changes from incidental stress encounters and responses, long-term effects may be primarily influenced by chronic stressors and relatively stable personality, coping and social support characteristics. Also the strength and direction of relationships between stress and vulnerability factors and disease activity may vary over time and be different for short and long-term outcomes. Some effects may become evident only in the long term and factors may even work in opposite directions in different time periods, e.g. due to a biphasic pattern of immunological or behavioral responses that is differently related to disease activity during and after the occurrence of major stress (Mullen & Suls, 1982; Koehler, 1985; Suls & Fletcher, 1985; McFarlane & Brooks, 1990; Huyser & Parker, 1998). Finally, effects may also depend on the stages of disease assessed (McFarlane & Brooks, 1990; Huyser & Parker, 1998). Preliminary evidence suggests that stressors and vulnerability factors are differently related to physical and psychological symptoms in early and long-standing RA (Smith et al., 1997), possibly due to changes brought about by the disease itself. Stressors and vulnerability factors in established RA have been shown to be affected by the inflammatory processes of the disease, its biopsychosocial consequences and the pharmacological treatment with prolonged medication (Evers et al., 1997; Fex et al., 1998; van Jaarsveld et al., 1998, 2000; Penninx et al., 1999), and they may be consequently more validly assessed in recently diagnosed patients (Zautra et al., 1989; Smith et al., 1997; Huyser & Parker, 1998).

The purpose of the present study was to examine the role of stress-vulnerability factors for their ability to predict long-term changes in disease activity in recently diagnosed RA patients. Specifically, we studied the relative contribution of personality characteristics (neuroticism and extraversion), physical and psychological stressors (chronic disease-related stressors of functional disability, pain, and disease impact on daily life, as well as major life events), coping and social support at the time of diagnosis to changes in disease activity 1, 3 and 5 years later. In line with preliminary evidence suggested by current theories and research, it was hypothesized that a more unfavorable course in disease activity after 1, 3 and 5 years could be directly predicted by personality characteristics of more neuroticism and less extraversion, higher levels of physical and psychological stressors, more passive avoidant coping, less active problem-focused coping and less social support at the time of diagnosis. In addition to these direct effects, several mediator and moderator effects were exploratively investigated. First, the mediating function of coping and social support for the relationship between personality characteristics and change in disease activity and for the relationship between stressors and change in disease activity was examined. In addition, the mediation function of stressors for the relationship between personality characteristics and change in disease activity, and of coping for the

relationship between social support and change in disease activity, was explored. Hypotheses of moderator effects included the moderating function of stressors on vulnerability factors, anticipating that the maladaptive effects of major life events and chronic disease-related stressors on disease activity would be greater in patients with more unfavorable personality characteristics, coping and social support. Moreover, moderator effects of the presence of the rheumatoid factor on all stressors and vulnerability factors were examined, assuming that the relationships of stressors and vulnerability factors to the course of disease activity might be stronger in patients with a negative rheumatoid factor. Finally, possible mediator and moderator effects between demographic variables (gender, age and educational level) and all stress-vulnerability factors were explored.

METHODS

Sample and Procedure

The sample consisted of outpatients with recently diagnosed RA from five hospitals in the Netherlands. All patients participated in one of two medical trials of second-line antirheumatic drugs (van Jaarsveld et al., 2000; van Everdingen et al., 2002). Inclusion criteria for the medical trials were a minimum age of 18 years, diagnosis according to the 1987 American College of Rheumatology (ACR) criteria (Arnett et al., 1988), and a duration of disease of less than one year. All incoming patients from the hospitals who met the inclusion criteria were asked to participate in the medical trials. About 25% of the patients did not agree to be randomized, but there were no differences found between these patients and participants in terms of their levels of disease activity. From the remaining 394 patients participating in the medical trials, a subgroup of 100 patients were randomly selected for participation in the present study.

Patients were informed about this study by their rheumatologists during their first visit, when ACR criteria were assessed. About three weeks later (range 0-12 weeks), clinical and self-report data were assessed during their second visit. This second visit was also the starting point for the prospective medical trials. Five patients did not return the questionnaires at this assessment point, resulting in 95 patients who participated in the present study at the time of diagnosis. In addition to assessing clinical and self-report data at the beginning of the study (Evers et al., 1997), data on disease activity, functional disability, and pain was again collected at the 1, 3 and 5-year follow-ups.

Of the 95 patients who correctly completed self-report data at the first assessment, 78 patients (82%) completed all assessment points during the 5-year study period. Participants in the follow-up were predominantly female (69%), married or living with a partner (76%), and had a primary (32%) or secondary

(57%) educational level. Mean age at the time of entering the study was 57 years (range 20-82 years). The rheumatoid factor was positive for 50 patients (64%). In terms of dropouts, 7 patients died, 2 moved, 1 was in remission and not longer treated in the rheumatology outpatient clinic and 7 did not complete the questionnaires for the follow-up assessments. When entering the study, dropouts did not significantly differ from participants in terms of demographic variables (sex, age, marital status, educational level), presence of the rheumatoid factor, disease activity, pain, functional disability, disease impact on daily life, experience of major life events, personality dimensions of extraversion, coping or social support. However, dropouts scored higher on the personality dimension of neuroticism than patients who completed all assessment points ($t = 2.87$, $p < 0.01$).

When included in the medication trials, all patients were randomly assigned to one of the medication strategies. The drug trials lasted at least two years for all patients, but medication strategies were continued unless adverse reactions or ineffectiveness made discontinuation inevitable in the opinion of the attending doctor. In that case, one of the other medication strategies from the trials was usually prescribed. The distribution of medication strategies was as follows: 30% and 23% of the patients used non-steroidal anti-inflammatory drugs (NSAID) alone at first assessment and at the 5-year follow-up, respectively; the other patients took NSAID in combination with methotrexate (30% and 49%, respectively), intramuscular gold (14% at both assessment points), hydroxychloroquine (15% and 9%, respectively), prednisone (11% and 1%, respectively) or other second-line medication, prescribed only for individual patients (4% at the 5-year follow-up). At the 5-year follow-up, 31% of the patients still used the initially prescribed medication, 65% used another medication strategy from the drug trial, and 4% of the patients used another second-line medication than those used in the medication trials. Finally, none of the patients in the psychosocial study met removal criteria during the study period, i.e. the occurrence of other serious disease processes or an incorrect RA diagnosis.

Measures

Demographic variables were assessed with a general checklist, assessing patients' gender, age and educational level. Educational level was measured using 7 categories that can be classified as primary, secondary and tertiary educational levels, representing an average of 7, 12, and 17 years of education, respectively.

Disease activity was determined by Erythrocyte Sedimentation Rate (ESR; 1-140mm first hour), an indicator of inflammatory activity, and by joint score ratings of the simultaneous presence of swelling and tenderness in 38 joints (range 0-534; Thomson, 1987). A composite score of both measures was used as an indicator of disease activity, in accordance to regular use of composite scores of disease activity that consist of at least ESR or another acute phase reactant and a joint score (van der Heijde et al., 1990, 1992; Prevoo et al., 1995). The composite score

was calculated by adding the standardized scores (*z*-scores) of both indicators (actual range between -2.32 and 3.25). A higher composite score indicates higher levels of disease activity.

Rheumatoid factor was determined by a latex fixation test or Rose-Waaler test, for which the result is positive in < 5% of healthy control subjects.

Functional disability was assessed using a composite score of one clinical measure and two self-report measures (Evers et al., 1998a). The clinical measure consisted of grip strength assessments with a Martin vigorimeter (the mean of three measurements on both hands was calculated). Self-reported functional disability was assessed with the Mobility and Self-care scales of the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL; Huiskes et al., 1990a, Evers et al., 1998b). The IRGL is derived from the Arthritis Impact Measurement Scales (AIMS) and assesses physical, psychological and social health in patients with rheumatic diseases. Previous research has shown that the reliability and validity of the IRGL scales are highly satisfactory (Huiskes et al., 1990a, Evers et al., 1998b). Items in the IRGL scales are scored on a 4-point or 5-point Likert scale. The Mobility and Self-care scales assess the functional capacities of the lower and upper extremities, respectively, over the last month (15 items). Cronbach's alpha in the present study was 0.89 for both scales. A composite score of the clinical measure and the two self-report scales was calculated by adding the standardized scores (*z*-scores) of all three indicators. A higher composite score indicates higher levels of functional disability.

Pain was assessed with the IRGL Pain scale (6 items), measuring the severity and frequency of painful episodes and swollen joints and the duration of early morning stiffness in the last month. Cronbach's alpha in the present study was 0.88.

Disease impact on daily life was measured with the IRGL Disease Impact scale (10 items), which assesses the general impact of the disease on several areas of daily life (i.e. work, leisure, relationships, sexuality, eating). Cronbach's alpha in the present study was 0.87.

Major life events were measured with a Dutch version of the Life Experience Survey (LES), assessing the occurrence of 60 stressful events related to health, work, financial circumstances, relationships, living, and personal matters in the last 12 months (Sarason et al., 1978; van de Willige et al., 1985). To minimize confounding effects between major life events and disease impact on daily life, four disease-related events were excluded (occurrence of severe disease, important changes in health status, hospital admission, surgery).

Personality dimensions, i.e. neuroticism and extraversion, were measured with a Dutch version of the Eysenck Personality Questionnaire (17 and 12 items, respectively) (EPQ; Wilde, 1970; Eysenck & Eysenck, 1991). Cronbach's alphas in the present study were 0.90 for neuroticism and 0.79 for extraversion.

Coping strategies were assessed with the Utrecht Coping List (UCL; Sanderman et al., 1992; Schreurs et al., 1993), a well-documented coping questionnaire in the Netherlands (Evers et al., 1997, 2001a; Scharloo et al., 1998, 1999), adopted from Westbrook (1979), which measures on a 4-point Likert scale active and passive coping strategies when dealing with everyday problems. Active coping was assessed with the Problem-focusing scale (7 items), measuring cognitive and behavioral efforts to apply goal-oriented problem-solving strategies (analyzing problems from various perspectives, generating different solutions, taking goal-oriented action, perceiving problems as a challenge). Passive coping was measured with the Avoidance scale (8 items), measuring cognitive and behavioral attempts to avoid, escape and acquiesce when facing everyday problems (giving in to avoiding and escaping difficult situations, withdrawing from situations, letting matters take their course, waiting to see which way the wind blows). Cronbach's alphas in the present study were 0.85 for the Active and 0.67 for the Passive coping scales.

Social support in the past six months was measured with the IRGL social functioning scales, reflecting quantitative and qualitative aspects of social support. The quantitative aspect was assessed by the size of the social network, i.e. the number of friends and family members with whom patients associate. The qualitative aspect was measured by the Perceived Support scale (5 items), inquiring about perceived availability of emotional and instrumental support (availability to share sad and pleasant events, get support when faced with stress and pain, get help for casual work). Cronbach's alpha for the Perceived Support scale in the present study was 0.88.

Statistical Analyses

To study mean linear changes in clinical status over time in the group of RA patients, analyses of variance with repeated measurements were performed for the indicators of clinical status (disease activity, functional disability, pain), using the variables at the different assessment points as dependent variables, followed by posthoc tests in the case of significant linear changes. To explore the relationship between stress-vulnerability factors at the time of diagnosis and changes in disease activity after 1, 3 and 5 years, Pearson correlation coefficients were calculated between the stress-vulnerability factors at the time of diagnosis and the residual gain scores for disease activity at the 1, 3 and 5-year follow-ups (Kerlinger, 1975). Sequential regression analyses were then performed to examine the relative contribution of stress-vulnerability factors (including demographic variables) to disease activity at the 1, 3 and 5-year follow-ups. Disease activity at the 1, 3 and 5-year follow-ups were used as dependent variables. In the first step, disease activity assessed at the time of diagnosis was entered, followed by the predictors significantly related to disease activity at at least one follow-up assessment. Mediating effects were determined with the procedure described by MacKinnon

and Dwyer (1993), calculating the difference between the regression coefficients of the unadjusted and adjusted (for the mediator) independent variable and dividing this mediated effect by the standard error of the mediated effect. Moderating effects were explored by calculating centered interaction terms between the predictor and the moderator and entering them in the regression analyses, after controlling for their main effects. Due to the relatively large number of explorative tests performed in these moderator analyses, a more conservative threshold of $p < 0.01$ was used. Finally, to control for possible confounding effects of medication, Pearson correlation coefficients were calculated between the use and duration of intake of every medication strategy separately (use vs. non-use) and the residual gain scores of disease activity at the 1, 3 and 5-year follow-ups.

Table 1 Means and SDs of Disease Activity Measures at the Time of Diagnosis and at the 1, 3, and 5-Year Follow-ups

	ESR		Joint score	
	M	SD	M	SD
Diagnosis	29.4	22.3	97.5	100.7
1-year follow-up	23.6	22.4	66.7	75.7
3-year follow-up	17.7	13.2	63.4	90.4
5-year follow-up	20.0	14.7	73.1	110.6

RESULTS

Change in Clinical Status during the Study Period

Disease activity scores at the time of diagnosis were in the normal range for representative samples with recent onset or longstanding RA (Huiskes et al., 1990a; Meenan et al., 1991; Evers et al., 1998b). During the 5-year period, there was a significant mean decrease in disease activity ($F(3,73) = 22.2$, $p < 0.001$ and $F(3,73) = 10.6$, $p < 0.01$ for the ESR and joint score, respectively; see Table 1 for means and standard deviations during the study period). In addition, chronic-disease-related stressors of pain and functional disability (grip strength) significantly decreased within 5 years after diagnosis ($F(3,75) = 9.6$, $p < 0.01$ for pain; $F(3,75) = 14.5$, $p < 0.001$ for grip strength). Post-hoc tests indicated that this improvement in clinical status was most obvious in the first year of the disease: all indicators markedly decreased in this year ($t = 3.06$, $p < .01$ for ESR; $t = 3.25$, $p < 0.01$ for the joint score; $t = 2.20$, $p < 0.05$ for pain; $t = 4.29$, $p < 0.001$ for grip

strength), possibly due to the beneficial effects of medication (van Jaarsveld et al., 2000; van Everdingen et al., 2002). After the first year of the disease, clinical status remained relatively stable, as indicated by nonsignificant posthoc tests between 1 and 3 and between 3 and 5 years, with one exception: an indicator of disease activity, ESR, significantly decreased further between the 1 and 3-year follow-ups ($t = 3.11$, $p < 0.01$).

Correlates of Disease Activity at the Time of Diagnosis

Pearson correlation coefficients showed that the composite disease activity score was significantly related to higher levels of functional disability, pain, and disease impact on daily life at the time of diagnosis ($r = 0.46$, $p < 0.001$; $r = 0.43$, $p < 0.001$; $r = 0.30$, $p < 0.01$, respectively). In contrast, nonsignificant relationships were found between disease activity and presence of the rheumatoid factor, major life events, personality dimensions of neuroticism and extraversion, coping and social support at the time of entering the study.

Table 2 Correlations between Rheumatoid Factor and Stress-Vulnerability Factors at the Time of Diagnosis and Changes in Disease Activity after 1, 3, and 5 Years [a]

	Change in disease activity		
	1 year	3 years	5 years
Rheumatoid factor	.25*	.23*	.22
Personality characteristics			
Neuroticism	.08	.12	.12
Extraversion	-.15	-.19	-.03
Stressors			
Physical stressors			
Functional disability	.14	.14	.06
Pain	.08	.04	-.02
Psychological stressors			
Disease impact on daily life	.00	-.13	-.19
Major life events	-.14	-.07	-.17
Coping			
Active problem solving	.02	-.08	-.03
Passive avoidance	.13	.33**	.28*
Social support			
Social network	.02	-.26*	-.11
Perceived support	.07	-.24*	-.11

[a] A positive correlation indicates that a higher level of the stress-vulnerability factor is related to an increase in disease activity (residual gain scores).
* $p < 0.05$ ** $p < 0.01$

Table 3 Multiple Regression Analyses Predicting Disease Activity at the 3 and 5-Year Follow-ups from Predictors at the Time of Diagnosis [a]

	Disease activity after 3 yrs.		Disease activity after 5 yrs.	
	β	ΔR^2	β	ΔR^2
Disease activity	.35**	.13**	.27*	.09**
Rheumatoid factor	.13	.05*	.15	.04
Coping		.07*		.05*
Passive avoidance	.30**		.25*	
Social support		.09*		.02
Social network	-.23*		-.11	
Perceived support	-.14		-.06	
Total ΔR^2		.34***		.20***

[a] Selection criterion for predictor variables was a significant correlation with changes in disease activity at least at a single follow-up assessment (see Table 2).
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$.

Predictors for Disease Activity at the 1, 3 and 5-Year Follow-ups

Correlation coefficients between the stress-vulnerability factors at the time of diagnosis and disease activity change scores at the follow-up assessments are presented in Table 2. At the 1-year follow-up, only the presence of the rheumatoid factor was related to an increase in disease activity, while stressors and vulnerability factors were all unrelated to changes in disease activity. At the 3 and 5-year follow-ups, significant correlations were found between coping and social support measures and changes in disease activity. The passive coping strategy of avoidance was significantly related to an increase in disease activity at the 3 and 5-year follow-ups. In addition, both social support measures (social network and perceived support) were inversely related to an increase in disease activity at the 3-year follow-up. No significant correlations were revealed between disease activity at follow-up assessments and other stress-vulnerability factors (personality dimensions, stressors and active coping) (see Table 2). In addition, demographic variables (gender, age, educational level) and the use or the duration of intake of the different medication strategies (NSAID alone, NSAID in combination with methotrexate, intramuscular gold, hydroxychloroquine, or prednisone) were not significantly related to changes in disease activity at the 1, 3 and 5-year follow-ups (data not shown).

Sequential regression analyses were performed to study the relative contribution of stress-vulnerability factors on changes in disease activity. Disease activity scores at the 1, 3 and 5-year follow-ups were used as dependent variables.

In the first step, disease activity at first assessment was entered, followed by the predictor variables that were significantly related to changes in disease activity at least at a single follow-up assessment point: presence of the rheumatoid factor, the passive coping strategy of avoidance and both social support indicators. In line with the results of the correlational analyses presented in Table 2, predictor variables of coping and social support did not significantly contribute to disease activity at the 1-year follow-up (data not shown). At the 3 and 5-year follow-ups, passive avoidance coping predicted a significant proportion of 7% and 5% of the variance in disease activity, respectively, after controlling for disease activity and the presence of the rheumatoid factor at the time of entering the study (see Table 3). Social support measures added 9% to disease activity variance at the 3-year follow-up, but failed to significantly predict disease activity at the 5-year follow-up. Beta coefficients for the final regression model showed that more avoidance coping predicted a more unfavorable course of disease at the 3 and 5-year follow-ups ($t = 2.99$, $p < 0.01$ and $t = 2.21$, $p < 0.05$, respectively), and a less extended social network predicted a more unfavorable disease course at the 3-year follow-up ($t = -2.19$, $p < 0.05$). Figures 1 and 2 illustrate the main findings, presenting the mean course of disease activity during the study period for patients with high vs. low levels of avoidance coping and social support (median split).

Mediator analyses overall indicated nonsignificant effects, failing to support a possible mediating function of stressors, coping and social support for the relationship between personality characteristics and changes in disease activity, of coping and social support for the relationship between stressors and changes in disease activity, of social support for the relationship between coping and change in disease activity as well as of stressors, coping and social support for the relationship between demographic variables and changes in disease activity at all assessment points (MacKinnon & Dwyer, 1993). In addition, moderator analyses of stressors on vulnerability factors, of the rheumatoid factor on all stress-vulnerability factors and of demographic variables on all stress-vulnerability factors showed that none of these interaction terms was significantly related to changes in disease activity at the 1, 3 or 5-year follow-ups, failing to support any moderating function for these variables on the course of disease activity.

DISCUSSION

The present study has examined the potential of stressors and vulnerability factors for predicting long-term disease activity in early RA. Contrary to expectations, none of the psychosocial factors assessed at diagnosis predicted short-term outcomes for disease activity after one year. This may be due to the fact that the newly prescribed medication at diagnosis seemed to be largely effective in

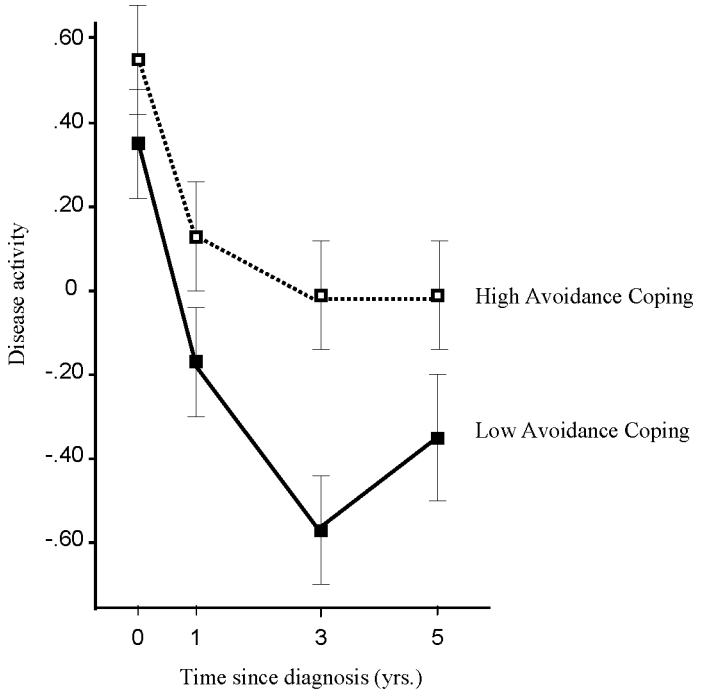

Figure 1 Mean course of disease activity for five years after diagnosis for patients with low versus high levels of avoidance coping at time of diagnosis (median split)

reducing disease activity, as indicated by the mean decrease in disease activity in the first year and as proved in previous trials of second-line anti-rheumatic medication (Felson et al., 1990; van Jaarsveld et al., 2000; van Everdingen et al., 2002), and these generally beneficial medication effects may have overshadowed the effects of the stress-vulnerability factors on short term changes in disease activity after one year. However, the vulnerability factors of coping and social support were related to the long-term course of disease activity after 3 and 5 years. Specifically, greater use of passive avoidance coping was a prognostic marker for a more unfavorable course of disease activity after 3 and 5 years. In addition, a less extended social network was predictive for a more unfavorable course of disease activity after three years, suggesting overall that psychosocial factors can affect long-term RA disease activity, regardless of the influence of biomedical factors or use of medication.

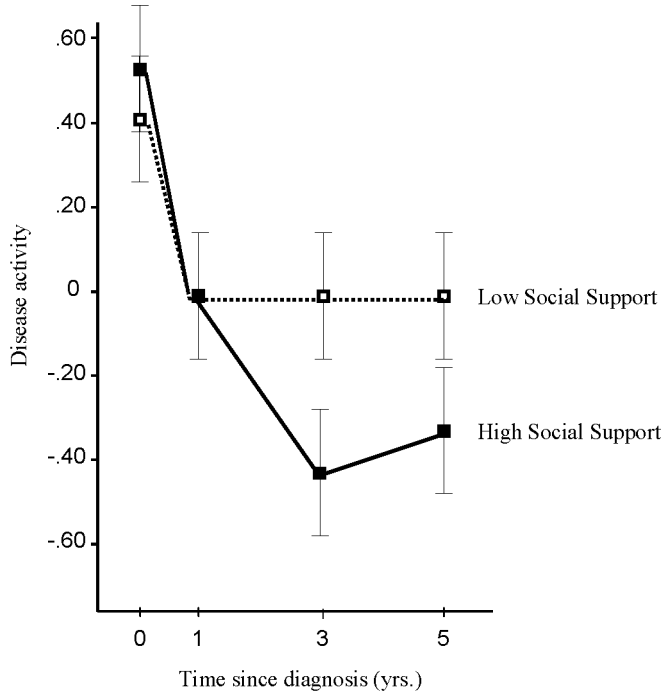

Figure 2 Mean course of disease activity for five years after diagnosis for patients with low versus high levels of social support at time of diagnosis (median split of composite score)

The relationships found between passive avoidance coping and the long-term course of disease activity after 3 and 5 years are in line with previous findings in RA patients and the general population. Passive avoidance coping has repeatedly been found to prospectively predict self-reported psychological and physical outcomes in RA patients (Brown & Nicassio, 1987; Evers et al., 1998a; Scharloo et al., 1999). In addition, avoidance coping has previously been reported to predict an exacerbated, long-term course of clinically assessed disease activity in RA patients (McFarlane et al., 1987), supporting the present finding that a general tendency to avoid and acquiesce to everyday problems could unfavorably affect disease activity in the long-term. The detrimental long-term effects are also in line with research in the general population, showing that avoidance can have beneficial effects on short-term outcomes but works unfavorably on various psychological and physiological outcomes in the long-term (Mullen & Suls, 1982; Suls & Fletcher,

1985). Independently of coping, social support predicted changes in disease activity at the 3-year follow-up. Specifically, a less extended social network was predictive for increased disease activity at the 3-year follow-up, but not at the 5-year follow-up. Although the relationship between social support and the course of disease activity was found at only one assessment point, the results are in line with general findings that social support indicators favorably affect long-term physical health outcomes in both chronically ill and healthy populations (Broadhead et al., 1983; Kaplan & Toshima, 1990; Uchino et al., 1996). In addition, there is some evidence that social factors are particularly relevant to RA disease activity, possibly due to the multiple consequences of RA on social relationships, such as increased dependency on others and decreased participation in social activities (Fex et al., 1998; van Jaarsveld et al., 1998; Penninx et al., 1999). For example, interpersonal stress factors have previously been reported to be related to disease fluctuations in RA patients (Potter & Zautra, 1997; Zautra et al., 1997, 1998), and the quality of spousal support has been shown to buffer short-term fluctuations of immunological parameters in periods of interpersonal stress (Zautra et al., 1998).

Previous studies in RA patients and the general population provide preliminary support for possible pathways linking avoidance coping and social support to increased disease activity in the long term. Passive avoidance coping has been shown to be related to specific neuroendocrine and immune responses (Steptoe, 1991b; Dantzer, 1993), and it might, for instance, affect RA inflammation because it changes cellular and humoral immune responses. Evidence has also been reported in general and chronically ill populations of direct and buffering beneficial effects of social support on immunological parameters, such as more proliferative T cells or natural killer cells (Broadhead et al., 1983; Uchino et al., 1996). One RA study supplied preliminary support for possible immunological pathways linking social support to disease activity, e.g. as a buffering factor for chronic interpersonal stress on T-cell activity (Zautra et al., 1998). Besides physiological pathways, cognitive-behavioral processes have been assumed to be crucial to explaining the relationship between coping and social support and the long-term course of disease activity (Broadhead et al., 1983; Steptoe, 1991a; Wills & Fegan, 2001). For example, passive avoidance coping and less social support have been shown to be related to cognitions of greater disease-related helplessness, less acceptance and less coping efficacy, which in turn have been demonstrated to concurrently or prospectively predict clinical indicators of disease activity or immunological parameters in RA patients (Zautra et al., 1989, 1994; Parker et al., 1991; Evers et al., 2001a). In addition, behavioral pathways may be responsible for increased disease activity, since passive avoidance coping has been shown to be related to less favorable health behavior, such as reduced adherence to medical recommendations (Sherbourne et al., 1992), while higher levels of support have been shown to be related to less maladaptive disease-related coping in RA (Manne & Zautra, 1989). Other cognitive-behavioral processes, such as paying less

attention to physical signals and consequently displaying less health-promoting behavior, may likewise be prominent in patients with high avoidance coping and less social support, and may figure as additional mediators in relationship to disease activity (Steptoe, 1991a; Wills & Fegan, 2001).

In contrast to the results of coping and social support, other stress-vulnerability factors of stressors, such as chronic, disease-related stressors, major life events and the personality characteristics of neuroticism and extraversion, failed to demonstrate any direct, mediating or moderating effects on the course of disease activity over time. Nonsignificant results between the personality characteristics of neuroticism and extraversion and the course of disease activity seem to support previous findings that patients scoring particularly high on neuroticism tend to report higher levels of self-reported psychological and physical symptoms, without suffering from worse clinical outcomes (Costa & McCae, 1987; Watson & Pennebaker, 1989; Affleck et al., 1997). With regard to stressors, however, a previous study have provided preliminary evidence of relationships between major life events and the short-term course of disease activity (Potter & Zautra, 1997). One reason for the nonsignificant relationship between major life events and the long-term course of disease activity in our study could be that major events affect more short-term fluctuations of disease activity than coping and social support, and more statistical power may be needed to detect the long-term consequences. The role of chronic, minor and interpersonal stressors that have previously been shown to be concurrently or prospectively related to the course of disease activity (Affleck et al., 1997; Potter & Zautra, 1997; Zautra et al., 1997), may be an additional factor in how stress might affect RA disease activity in the long-term, directly or as a modifying factor for coping and social support on long-term disease activity (Zautra et al., 1998). Finally, there was no evidence suggesting that the relationship between psychosocial factors and disease activity was more evident in subgroups of patients with a negative rheumatoid factor, for whom RA is possibly less genetically determined.

Our prospective study offers several advantages for assessing the relationship between various stressors and vulnerability factors and clinical indicators of disease activity across several points in time in a sample of recently diagnosed patients, while simultaneously controlling for confounding biomedical factors. However, several of the study's limitations should be recognized. The study might contain some selection bias, as all patients participated in medical trials and dropouts obtained somewhat higher scores on neuroticism than participants. Posthoc analyses indicated that neuroticism was significantly related to more passive avoidance coping ($r = 0.35$, $p < 0.01$) at study entry, but not to indicators of social support. Consequently, the generalizability of the findings for passive avoidance may be limited to patients characterized by only moderate levels of passive avoidance coping. However, this finding could also have led to an underestimation of the effects of passive avoidance on disease activity. Prospective

research is inherently threatened by aspects of internal validity, and unmeasured biomedical or psychosocial factors may account for effects on disease activity. For example, the lack of short-term effects for psychosocial variables at the 1-year follow-up may be due to the specific stress situation patients are confronted with at the time of diagnosis. In addition, other stressors and vulnerability factors not measured in our study may account for changes in long-term disease activity, e.g. interpersonal stressors that have previously been shown to be related to the course of disease activity (Affleck et al., 1997; Potter & Zautra, 1997; Zautra et al., 1997, 1998). Moreover, although the sample was comparable to other samples with recent and longstanding RA and the mean decrease in disease activity is in accordance with what is usually found in recent and longstanding RA when applying second-line anti-rheumatic medication, the predictive capacity of coping and social support on long-term disease activity may be limited to a reduction in disease activity at an early stage of the disease. Finally, the relatively general assessment of coping and social support and the lack of assessment of possible mediators limit the opportunity to draw conclusions about the specific pathways through which coping and social support may affect disease activity.

Regardless of these limitations, our findings suggest that coping and social support affect long-term disease activity in early RA. Previous studies have shown that psychosocial treatments geared to modifying cognitive, behavioral or social stress responses can beneficially affect markers of disease activity in RA patients (Bradley et al., 1987; Radojevic et al., 1992), suggesting that an unfavorable course of disease may be modified by psychosocial factors. Our results further suggest that psychosocial vulnerability factors that predict a worse long-term course of disease are already established at the time of diagnosis, and early treatment for patients at risk may have a lasting impact on disease activity (Smith et al., 1997). With increasing knowledge of underlying mechanisms, psychosocial screening at diagnosis followed by psychosocial interventions for patients at risk may be used as an adjunctive strategy to standard biomedical RA treatment.

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3

3.1 Coping and Social Support

3.1.2 Predictors of functional disability and pain

3.1.2.1 Psychosocial predictors of functional change in recently diagnosed rheumatoid arthritis patients

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ABSTRACT

In order to examine the influence of active and passive pain coping strategies and social support characteristics on the change in functional status in the first stage of the disease in rheumatoid arthritis patients, self-report data and clinical and laboratory measures were collected of 91 patients (70% female, mean age 57 years) shortly after diagnosis and one year later. Multiple regression analyses indicated that, after taking the influence of demographic variables, disease activity and pain into account, a decrease in functional status (mobility, self-care, grip strength) after one year could be predicted by an initially more frequent use of the passive pain coping strategies of worrying and resting. A decrease in mobility could be additionally predicted by an initially smaller social network. Results indicate the impact of passive pain coping strategies and social network characteristics for the prognosis of functional outcome in the first stage of the disease and suggest the early manifestation of avoidance mechanisms, including behavioral, cognitive-emotional and social components, in face of a chronic stressor.

INTRODUCTION

Functional disability is a major concern in rheumatoid arthritis (RA), a chronic, unpredictive disease, which affects about 1% of the western population. Already in the first year of the disease, functional disability is established (Meenan et al., 1991), and it progressively deteriorates with an ongoing disease duration (Sherrer et al., 1986; Wolfe & Cathey, 1991). In addition, functional disability in the first year of the disease has been shown to be a prognostic marker for work loss at 2-year follow-up (Eberhardt et al., 1993), for a worse prognosis at 10-year follow-up (Sherrer et al., 1986) and for future mortality at 15-year and 20-year follow-up (Rasker & Cosh, 1989; Corbett et al., 1993). As causal treatment of the disease is not available, therapy is primarily focused on the alleviation of the symptoms and the maintenance of functional status. Identifying mechanisms that affect the process of ongoing disability in an early state of the disease might be therefore highly desirable to predict and possibly prevent an unfavorable long-term outcome in RA patients.

In accordance to the WHO (1980), disability can be defined as difficulties in performing activities of daily living resulting from the disease which leads to impairment (pain, stiffness, restricted joint movement) and hence to disability. However, disease factors modestly predict future disability in early and longstanding RA (e.g., Wolfe & Cathey, 1991; van der Heide et al., 1995), which raises the question about the possible influence of psychosocial factors. The concept of avoidance offers a theoretical framework through which psychosocial factors affect the functional outcome (e.g. Philips, 1987; Dekker et al., 1992). The avoidance of activity is a natural and adaptive reaction to the sudden experience of pain (Wall, 1979), which becomes maladaptive when it is continuously used (Mullen & Suls, 1982; Suls & Fletcher, 1985; Holmes & Stevenson, 1990). Due to expectancies of increased pain (McCracken et al., 1993; Crombez et al., 1996), attention to symptoms (Crombez et al., 1995), and fear of pain or movement (Crombez et al., 1995; Vlaeyen et al., 1995) avoidance behavior is reinforced, consisting of restriction activities and resting. A cognitive-emotional pattern of negative outcome expectancies and worrying is expected to promote the avoidance behavior and vice versa. A lack of support by the environment which is supposed to decrease the ability of an individual to cope with the stress of a chronic disease, may additionally enhance the avoidant behavior (Cohen & Wills, 1985; Manne & Zautra, 1989). Avoidance behavior may hence induce harmful long-term effects on physical functioning by limiting joint movement and inducing muscle weakness which leads to functional disability (Kottke, 1966; Dekker et al., 1992, 1993b). Research on psychosocial factors in general supports this theoretical framework, and there is reasonable evidence that the way of coping with pain and the receipt of social support affect the functional status of RA patients, at least in relatively

established and longstanding RA and other chronic pain populations, such as patients with osteoarthritis or chronic pain patients.

With regard to pain coping strategies, it can be concluded that specifically the absence of avoidance-oriented, passive coping strategies is related to a better functional status over time, while an adaptive function of active strategies has been less frequently demonstrated. Apart from suggestive evidence of studies measuring these relationships at one point in time (see for a review, Jensen et al., 1991b; Manne & Zautra, 1992), longitudinal studies in RA patients have yielded some promising results. For example, Brown and Nicassio (1987) have demonstrated that the greater use of passive pain coping strategies (tendency to depend on others, to engage in wishful thinking and to restrict one's functioning) predicted less physical activity and activities of daily living six month later, while a more frequent use of active pain coping strategies (attempts to distract oneself from the pain and to function in spite of the pain) predicted higher physical activity at 6-month follow-up. Keefe et al. (1989) found that a greater use of the strategy catastrophizing predicted worse functional disability six month later. Revenson and Felton (1989) have demonstrated that an increased use of wish-fulfilling fantasy was related to increased physical disability after six months. In other chronic pain conditions, namely, sickle cell disease, Gil et al. (1992) reported that negative thinking (e.g. catastrophizing) and passive adherence (e.g. resting) were associated with greater activity reductions during the subsequent nine months. In addition, increase in this passive coping strategy was related to further reductions in the activity level during painful episodes.

In literature on social support it is assumed that social resources affect the health status of patients by enhancing the ability of an individual to cope with the stress of a chronic disease. Especially the functional, qualitative aspects of social support, such as the perceived availability of support, have been assumed to be more important in patients with a chronic stressor than structural, quantitative characteristics of an individual's support system, such as the size of the social network (Cohen & Wills, 1985). Research indeed demonstrated a link between social influences and functional status. Several studies reported that married RA patients have less functional disability (Verbrugge et al., 1991) and less progression of functional disability over the disease course than never married, divorced or widowed patients (Leigh & Fries, 1992; Ward & Leigh, 1993). In line with Cohen and Wills (1985), research in RA patients and other chronic pain populations suggest that this link may be mainly due to the qualitative aspects of social support. While the size of the social network was not related to functional status (Brown et al., 1989b) or its change within one year (Smedstad et al., 1995) in RA patients, Brown et al. (1989b) reported that the quality of emotional support was negatively related to functional disability at three measurement points within one year. In addition, Weinberger et al. (1990) demonstrated in osteoarthritis patients that physical disability was negatively related to the perceived availability

of (tangible) support. In chronic pain patients, Jamison and Virts (1990) found that patients who perceived a greater lack of support from their families had more activity limitations at 1-year follow-up than patients who felt supported by their families.

The extent to which the contribution and the adaptiveness of these pain coping strategies and social support characteristics on functional status can be generalized with respect to the first stage of the disease is questionable, as patients have to cope with different stressors and physical mechanisms in early and longstanding RA. However, the kind of stressors and physical mechanisms may suggest that avoidance mechanisms are already established at an early stage of the disease. In contrast to later phases of the disease, when joint damage is at stake and disability increases more regularly and slowly, functional status in early RA is predominantly affected by acute phases of inflammatory activity (Guillemin et al., 1992; Eberhardt & Fex, 1995). In addition, shortly after diagnosis patients are rather inexperienced in dealing with the disease, have less knowledge about possible noxious long-term effects of coping strategies, and may also be overwhelmed by negative emotions due to the new confrontation with a chronic disease. These kinds of stressors and physical mechanisms probably promote the use of strategies which have benefits in the short-term. The short-term effectiveness may enforce avoidance mechanisms with deteriorating long-term effects on functional status. In the case of low levels of social support, patients may even rely more on avoidant patterns with additional maladaptive long-term effects on functional status.

In order to determine these possible effects of psychosocial predictors on change in functional status in the first stage of the disease, we examined the predictive value of active and passive pain coping strategies and social support characteristics on change in self-report and clinical measures of functional status in the first year after diagnosis in rheumatoid arthritis patients. In accordance to the theoretical approach and empirical evidence in longstanding RA, it was hypothesized that a deterioration in functional status after one year could be predicted from an initially more frequent use of passive pain coping strategies and initially lower levels of social support.

METHODS

Participants

The sample consisted of successive outpatients with recently diagnosed RA from five hospitals in the Utrecht area, the Netherlands. Patients were participating in a prospective study on the effects of different medication strategies (van der Heide et al., 1996). Inclusion criteria were a minimum age of 18 years, a disease duration of less than one year, and a diagnosis of RA assessed by a rheumatologist

according to the 1987 American College of Rheuamtology (ACR) criteria (Arnett et al., 1988). Patients were informed by their rheumatologists about this study during the first routine visit in which ACR criteria were assessed. One-hundred patients agreed to participate and received a questionnaire during the second routine visit which was scheduled about three weeks later (range 0-12 weeks). This second visit was also the starting point for the second-line anti-rheumatic medication. Correctly completed questionnaires were returned by 95 patients. One year later, 91 patients completed the questionnaires again. None of the patients had a spontaneous remission of the disease. The sample was predominantly female (70%), married or living together with a partner (74%), with primary (34%) or secondary (53%) education. The mean age was 57 years (range 20-82 years). The medication of the patients was as follows: 31% patients were only on non-sterodial anti-inflammatory drugs (NSAID); the other were on NSAID in combination with methotrexate (25%), intramuscular gold (16%), hydroxychloroquine (14%), or prednisone (14%).

Measures

Functional status was assessed by three variables, including clinical and self-report data. The clinical measurement was grip strength assessed by a Martin vigorimeter (mean of three measurements of each hand was calculated). Self-reports of functional status were measured by the physical functioning scales of the Impact of Rheumatic diseases on General health and Lifestyle (IRGL; Huiskes et al., 1990a). The IRGL is partly derived from the Arthritis Impact Measurement Scales (AIMS; Meenan et al., 1980) and assesses the physical, psychological and social aspects of health status in patients with rheumatic diseases. The Mobility (7 items) and Self-care (8 items) scales measure functional status in the past month, assessing the use of lower and upper extremities, respectively. Items of the IRGL scales are scored on a 4-point or 5-point Likert-scale. In previous research, reliability and validity of the IRGL scales were shown to be highly satisfactory (Huiskes et al., 1990a), and the physical functioning scales have been demonstrated to be highly comparable to the corresponding scales of the Dutch version of the AIMS2 (Evers et al., 1998b).

Disease activity was assessed through standardized clinical and laboratory measurements. Data were collected on erythrocyte sedimentation rate (ESR), an indicator of the inflammatory activity, and on joint score (number of swollen and painful joints; Thompson et al., 1987).

Pain in the last month was assessed by the Pain scale (6 items) of the IRGL asking about the severity and frequency of painful episodes and swollen joints and the duration of morning stiffness.

Social support in the past six months was measured by the social functioning scales of the IRGL, reflecting a quantitative and qualitative aspect of social support. The quantitative aspect was assessed by the size of the social network, that

is the number of friends one associates with (including family members). The qualitative aspect was measured by the scale Perceived Support (5 items), asking about the perceived availability of emotional and instrumental support (availability to share sad and pleasant events, to get support in face of stress and pain, to get help for casual work).

Pain coping strategies were assessed by the Pain Coping Inventory (PCI; Kraaimaat & Schevikhoven, 1988; Kraaimaat & Huiskes, 1989; Kraaimaat et al., 1997), measuring behavioral and cognitive strategies when dealing with pain. Patients are instructed to indicate the frequency with which they engaged in various kinds of behavior and thoughts in the face of pain on a 4-point scale ranging from 'rarely or never' (1) to 'very frequently' (4). Six independent pain coping strategies can be identified, representing an active or passive way of dealing with pain. Active pain coping strategies reflect cognitive and behavioral efforts to distract oneself from the pain (Distraction, 5 items; Pain Transformation, 4 items) and to function in spite of the pain (Reducing Demands, 3 items). Passive pain coping strategies reflect behavioral tendencies to restrict one's functioning (Resting, 5 items), to avoid environmental stimuli (Retreating, 7 items) and negative cognitions about the pain (Worrying, 9 items). An overall unweighted sumscore of the active and passive pain coping strategies can be calculated. Confirmatory construct and criterion validity of the scales and of the second-order structure with respect to active and passive pain coping strategies were supported in previous research on RA patients, patients with chronic headache and patients attending pain clinics (Kraaimaat et al., 1997). The following Cronbach's alpha coefficients in RA patients were obtained: Pain Transformation, 0.75; Distraction, 0.69; Reducing Demands, 0.73; Retreating, 0.69; Worrying, 0.79; and Resting, 0.72.

Statistical Analyses

Due to skewed distributions of scores at ESR and joint score, square root transformations were applied. In order to examine the relative contribution of pain coping strategies and social support on change in functional status within one year, hierarchical multiple regression analysis was performed with all predictors which were significantly related to change in at least one of the measures of functional status (residual gain scores of mobility, self-care, grip strength). After taken into account the influence of the initial functional status (step 1), demographic variables (step 2) and disease activity (step 3) into account, pain coping strategies and social support were entered at steps 4 and 5. Bivariate associations between all variables were calculated with Pearson correlation coefficients. Differences between the means of the first and second assessment were tested with Student's *t*-test and Wilcoxon Signed Rank Test in the case of ESR and Thompson's joint score. All statistical analyses were carried out with the SPSS 6.1/Windows statistical package with a minimum of 88 patients sharing complete data sets.

Table 1 Functional Status, Disease Activity, Pain, Pain Coping Strategies, and Social Support Shortly After Diagnosis (T1) and 1 Year Later (T2)

Variable (range)	T1		T2		
	M	SD	M	SD	*p*-value [a]
Functional status					
Mobility (7-28)	19.6	6.1	20.9	5.7	0.003
Self-care (8-32)	24.3	5.9	25.3	5.6	0.112
Grip strength (0-130kPa)	32.7	23.0	40.4	26.2	0.000
Disease activity					
ESR (1-140 mm 1st hr)	30.9	23.3	23.7	22.4	0.000
Joint score (0-534)	96.9	95.9	66.0	77.4	0.000
Pain (6-25)	15.6	4.9	14.1	5.3	0.008
Pain coping					
Active (3-12) [b]	7.1	1.4	6.7	1.5	0.019
Pain transformation (4-16)	9.2	2.6	8.8	2.8	0.122
Distraction (5-20)	12.5	3.1	11.7	3.3	0.029
Reducing demands (3-12)	6.7	1.9	6.5	1.9	0.341
Passive (3-12) [b]	6.1	1.5	5.6	1.6	0.002
Resting (5-20)	11.9	3.1	11.4	3.3	0.097
Worrying (9-36)	17.4	5.6	15.5	4.9	0.000
Retreating (7-28)	12.2	4.0	11.6	4.2	0.051
Social support					
Social network (1-4) [c]	3.2	0.8	3.0	0.9	0.013
Perceived support (5-20)	16.6	3.6	16.4	3.6	0.568

[a] Two-tailed properties of *t*-test or Wilcoxon Signed Rank Test in the case of ESR and joint score.
[b] Unweighted sumscore.
[c] Categorized into norm classes (Huiskes et al., 1990a).

RESULTS

Change in Health Status, Pain coping and Social Support within the First Year After Diagnosis

The means and standard deviations of health status measures, pain coping strategies and social support characteristics of the patients shortly after diagnosis and one year later are presented in Table 1. As evident, the mean health status of patients improved within the first year after diagnosis, indicated by an increase in functional status (mobility and grip strength), a decrease in disease activity (ESR and joint score), and a decrease in pain. At the same time, the use of the total set of active and passive pain coping strategies was decreased within one year. More specifically, patients used the strategies of distraction and worrying, and tended to

use the strategies of resting and retreating less frequently. With regard to social support, the size of the social network decreased within one year. Patients reported having less friends one year after diagnosis than shortly after diagnosis, while the perceived availability of support was more or less constant.

Table 2 Pearson Correlation Coefficients with Measures of Functional Status Shortly After Diagnosis

	Mobility	Self-care	Grip strength
Demographic variables			
Sex	-.12	-.30**	.26**
Age	-.14	-.06	.06
Education	.06	.03	.00
Marital status	.05	-.13	-.03
Disease activity			
ESR	-.40***	-.28**	-.41***
Joint score	-.28**	-.28**	-.36***
Pain	-.23*	-.19	-.27**
Pain coping			
Active			
Pain transformation	.09	.07	.04
Distraction	-.06	-.29**	.00
Reducing demands	-.22*	-.07	-.02
Passive			
Resting	-.46***	-.34**	-.38***
Worrying	-.47***	-.32**	-.17
Retreating	-.43***	-.33**	-.08
Social support			
Social network	.08	.16	.09
Perceived support	.12	.17	.10

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$.

Correlates of Functional Status Shortly After Diagnosis and 1 Year Later

The relationship between functional status (mobility, self-care and grip strength) and demographic variables, disease activity, pain, pain coping strategies and social support shortly after diagnosis are presented in Table 2. Lowered functional status was significantly related to the female sex and to a higher level of disease activity and pain. In addition, the frequent use of passive pain coping strategies was strongly related to the self-report measures and to a lesser extent to

the clinical measure of functional status, indicating poorer functional status when using the strategies of retreating, worrying and resting more frequently. The use of active pain coping strategies was hardly associated with functional status, and the significant associations that were revealed, indicated a negative relationship with functional status: the use of distraction was related to lower levels of self-care, and the strategy of reducing demands was associated with lower levels of mobility. For measures of social support, no significant relationship could be revealed with functional status shortly after diagnosis.

One year after the diagnosis, the strength of the cross-sectional relationships between functional status and the predictors was somewhat different (data not shown). Consistent for all measures of functional status, the relationship with the joint score, an indicator of the disease activity, was hardly significant one year after diagnosis (only for grip strength, $r = 0.22$, $p < 0.05$), while the relationships with pain (mobility: $r = -0.43$; self-care: $r = -0.41$; grip strength: $r = -0.43$) and with the passive pain coping strategies (mobility: between 0.47 and 0.56; self-care: between 0.44 and 0.45; grip strength: between 0.22 and 0.44) were stronger than shortly after diagnosis. In addition, self-reports of functional status were also significantly related to the qualitative aspect of social support one year after diagnosis (mobility $r = 0.27$; $p < 0.01$ and self-care $r = 0.26$, $p < 0.05$), indicating a better functional status for patients who perceived a higher availability of support. All in all, while shortly after diagnosis functional disability scores were more strongly related to underlying disease processes, their relationship with pain, with the use of passive pain coping strategies and with the qualitative aspect of social support increased within one year.

Predictors of Change in Functional Status in the First Year After Diagnosis

In order to evaluate the extent to which the independent variables shortly after diagnosis predicted the individual patient's course of functional status within one year, a hierarchical multiple regression analysis was conducted with the functional status measures one year after diagnosis as dependent variables, entering functional status measures shortly after diagnosis at the first step. Only those variables were entered in the regression model which were significantly related to at least one of the outcome measures. For this purpose, residual gain scores of mobility, self-care and grip strength were calculated. Of the set of predictors, sex, ESR, the passive pain coping strategies of resting and worrying and the social network were significantly related to change in at least one of the measures of functional status (see Table 3). Hierarchical regression analyses revealed a strong autoregressive effect for the functional status measures over time, accounting for 53% of the variance in mobility (Fchange = 101.78, $p < 0.001$), for 29% in self-care (Fchange = 36.62, $p < 0.001$), and for 55% in grip strength (Fchange = 114.56, $p < 0.001$), indicating that functional status just after the RA diagnosis proved to be the best predictor of functional status one year later. At step 2, sex (being female)

contributed 2% to a decrease in grip strength (*F*change = 4.96, $p < 0.05$), and at step 3, an inital higher level of ESR accounted for a decrease in self-care of 3% (*F*change = 4.64, $p < 0.05$). At step 4, the passive pain coping strategies resting and worrying explained 3% of the variance to change in all measures of functional status (mobility: *F*change = 3.31, $p < 0.05$; self-care: *F*change = 3.17, $p < 0.05$, grip strength: *F*change = 3.99, $p < 0.05$), indicating a deterioration in self-reported and clinical functional status after one year when initially using the passive pain coping strategies of resting and worrying more frequently. Finally, at step 5, the size of the social network made an additional significant contribution of 3% to change in mobility (*F*change = 7.85, $p < 0.05$), indicating a further decrease in mobility in the event of an initially smaller social network. When the size of the social network was entered before the pain coping strategies, the results were the same as in the reversed order, suggesting that the use of pain coping strategies and the size of the social network independently affect the change in functional status.

All in all, a decrease in all measures of functional status within the first year after diagnosis could be predicted by the initially more frequent use of the passive pain coping strategies of resting and worrying. A decrease in mobility could be additionally predicted by an initially smaller social network, independent of what could be explained by the initial functional status, demographic variables or by the disease itself.

DISCUSSION

The present study provides information about psychosocial factors to identify those individuals likely to deteriorate in functional status in an early stage of the disease. Results suggest that behavioral and cognitive pain coping strategies and social resources affect the clinical and self-reported functional status of RA patients in the first year of the disease. Recently diagnosed RA patients who use passive pain coping strategies more frequently and who have a smaller social network, are at risk for loss of functional status within one year.

Within the set of the passive pain coping strategies, two strategies affect the development of the functional status, namely resting and worrying, representing behavioral and cognitive-emotional coping patterns in the face of pain. The maladaptive long-term effects of resting have been frequently suggested (e.g. Kottke, 1966; Brown & Nicassio., 1987; Dekker et al., 1992), and cross-sectional relationships between resting and higher levels of functional disability have been demonstrated in patients with longstanding RA (Kraaimaat & Huiskes; 1989) and other chronic pain patients (Jensen et al., 1991a; Hopman-Rock et al., 1998). Our results extend previous work by providing evidence that resting has indeed deleterious long-term effects on functional status over time, probably mediated by

Table 3 Stepwise Multiple Regression Predicting Functional Status 1 Year After Diagnosis (T2) from Selected Predictors at Study Entry (T1) [a]

	Mobility T2			Self-care T2			Grip Strength T2		
	r [b]	β	adj. ΔR^2	r	β	adj. ΔR^2	r	β	adj. ΔR^2
Functional status T1									
Mobility	0.73***	0.62***	0.53***						
Self-care				0.54***	0.37***	0.29***			
Grip strength							0.75***	0.63***	0.55***
Demographic variables									
Age	-0.14			-0.05			0.03		
Sex	-0.06	0.05	0.00	-0.12	-0.06	0.00	-0.23*	-0.14	0.02*
Education	0.06			0.01			-0.05		
Marital status	0.08			0.13			0.03		
Disease activity T1									
ESR	-0.16	-0.12	0.00	-0.24*	-0.17	0.03*	-0.13	-0.06	0.00
Joint score	-0.04			-0.12			-0.10		
Pain T1	0.05			-0.07			-0.07		
Pain-coping T1									
Active									
Pain transformation	0.00			0.00			0.01		
Distraction	0.02			0.04			0.07		
Reducing Demands	-0.03			-0.12			-0.06		
Passive			0.03*			0.03*			0.03*
Resting	-0.23*	-0.22*		-0.24*	-0.10		-0.25*	-0.10	
Worrying	-0.04	0.10		-0.26*	-0.15		-0.29**	-0.13	
Retreating	-0.12			-0.18			-0.15		
Social Support T1									
Social network	0.26*	0.20**	0.03**	0.16	0.14	0.01	0.11	0.02	0.00
Perceived support	0.02			0.11			0.02		
Total adj. ΔR^2			0.59***			0.36***			0.60***

[a] Selection criterion was the significant association with change in one of the measures of fucntional status (residual gain scores).
[b] Correlations with residual gain scores of functional status (except in the case of functional status measures T1).
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$.

physiological mechanisms, such as ensuing disuse of muscles and muscle weakness (Dekker et al., 1992, 1993b). These results are especially important, since resting is the strategy most frequently used in RA patients, outpatients of a pain clinic (Kraaimaat et al., 1997), and elderly people with chronic pain (Hopman-Rock et al., 1987), and is also evaluated as most effective in reducing pain (Kraaimaat & Huiskes, 1989). Although resting might be effective in the short run and be indicated in periods of disease flare-ups and active phases of the disease, its frequent use when the disease is declining probably causes harmful effects on functional disability (Kottke, 1966; Dekker et al., 1992, 1993b).

Apart from resting, the frequent use of worrying predicted a deterioration in functional status within one year. A relationship between similar constructs and functional disability has been frequently reported in RA patients, e.g. as coping factors which include catastrophizing (Hagglund et al., 1989; Keefe et al., 1989; Beckham et al, 1991, 1994) or wishful thinking (Parker et al., 1989; Revenson & Felton, 1989). The link with avoidance behavior (such as resting) may indicate that worrying is a strategy to remain vigilant and to direct attention to potential painful stimuli. Although this signal function may be adaptive for the experience of acute pain, the frequent use of worrying in the face of chronic pain, possibly linked to anticipatory anxiety processes such as fear of pain and an exaggerated attention to symptoms, has a negative effect on long-term functional status in early (this study) and more established RA (Keefe et al., 1989).

Our data give further support to the maladaptive long-term effects of passive pain coping strategies, and illustrate the early manifestation of avoidance behavior in the face of a chronic disease. In addition, the results permit the identification of specific kinds of avoidance behavior, namely the restriction of activities and worrying, that have deleterious long-term effects on functional status in early RA, while the passive pain coping strategy of retreating, measuring the avoidance of stimulation, did not affect functional status within one year, and seems to be less maladaptive for the development of functional disability in early RA. Although the explained variance of the predictors was rather small, results suggest that the link between avoidance behavior and functional status increases within the first years of the disease. While shortly after diagnosis functional disability was more strongly related to underlying disease processes, one year later its relationship with pain and the use of passive pain coping strategies increased. Such an increased relationship between avoidance behavior and pain with ongoing disease duration has also been reported in other chronic pain conditions (Philips & Jahanshahi, 1985), possibly suggesting that the contribution of avoidance behavior to functional status is a function of disease duration and that it becomes stronger within the course of the disease.

In contrast to the passive pain coping strategies, the active strategies were hardly related to functional status, and also did not predict its long-term change within one year, as has frequently been reported in longstanding RA and other

chronic pain conditions (see Jensen et al., 1991b). It is supposed that successful coping is not the consequence of using specific adaptive strategies, but an absence of the continuous use of maladaptive strategies, such as abstaining from, interrupting, and preventing avoidance behavior (e.g., Rosenstiel & Keefe, 1983; Turk & Rudy, 1992). Considering the fact that the functional status in early RA depends on inflammatory activity, and as a result patients have to cope with strong short-term fluctuations, the frequent attempts to control the pain or distract oneself from the pain may indeed not be beneficial when a continuous stressor is highly uncontrollable (Rosenstiel & Keefe, 1983). Adaptive coping in early RA may be reflected by flexible shifts between active and passive coping, adjusted to the demands of the stressor. Direct beneficial effects of the use of active strategies may occur in patients with relatively mild disease processes (Jensen & Karoly, 1991), be visible over the longer term (Mulen & Suls, 1982; Suls & Fletcher, 1985), and also be reflected in other outcome variables, such as a prolonged capacity to work, more independence in daily life and relatively less use of medication and health care facilities.

Of the measures of social support, the size of the social network shortly after diagnosis affected functional status within one year, indicating that patients with a smaller social network shortly after diagnosis are at risk of a decline in mobility in the first year of the disease. In line with the passive pain coping strategies, a smaller social network probably indicates an additional tendency to engage in avoidance behavior by limited social activities. Patients who have a more limited number of social network members are probably less sociable, make fewer visits and engage less in social activities which might induce harmful effects on their long-term mobility. In contrast to resting, these limited social activities only affect mobility of the patients and not self-care and grip strength (the use of upper extremities), which also explains previous nonsignificant findings of studies where composite disability scores were used (Smedstad et al., 1995). Results then suggest that, apart from the behavioral component of resting and the cognitive-emotional component of worrying, avoidance mechanisms in an early stage of the disease include an additional social component of limited social contacts which affect long-term disability in RA patients. In contrast to the quantitative aspects, qualitative aspects of social support, such as the perceived availability of support, may be less indicative of sociability, but rather enhance the ability of an individual to cope with the stress of a chronic disease, reinforce the use of more effective coping strategies (Manne & Zautra, 1989) and decrease the individual's tendency of his/her avoidance behavior and hence induce long-term effects on functional status. In our sample, the qualitative aspect of social support was associated in the cross-sectional analyses with self-report measures of functional status one year after diagnosis, but not shortly after diagnosis. A relationship between the qualitative aspects of social support and functional status has also been demonstrated in patients with more established arthritis (Brown et al., 1989b;

Weinberger et al., 1990), suggesting that qualitative aspects of social support become more important for the development of functional status in a later phase of the disease.

Our results have several implications for clinical practice. The identification of psychosocial factors which affect the long-term outcome in an early stage of the disease support the implementation of multidisciplinary treatment in an early stage of the disease, consisting of educational programs to inform patients early in the disease about the possible maladaptive effects of avoidance behavior, and of cognitive-restructuring and coping-skill training to teach individuals how they can most effectively stop and interrupt avoidance behavior when the disease is declining and develop compensatory strategies for engaging in activities. It also supports network- and activity-enhancing treatments, for example offering phone consultations, support groups, social activities or exercise therapy. Although most of these treatments have been applied to patients with more established RA, and beneficial effects on functional status have been demonstrated (e.g., Weinberger et al., 1986; Minor et al., 1989; Keefe et al., 1990a,b; Radojevic et al., 1992), their effects are rather small and most interventions failed to demonstrate a lasting effect at later follow-up (see for reviews, Dekker et al., 1993a; Keefe & Van Horn, 1993; Hawley, 1995; Taal et al., 1997). Establishing this treatment in early RA may be more effective. Considering that the coping repertoire is probably less established, it is easier to modify maladaptive coping patterns, learn an adaptive way to handle the consequences of the disease, and integrate this adaptive pattern in a life style. If the early phase of the disease is the critical one, when patients develop attitudes and patterns of long-term behavior and enduring patterns of adjustment, the modification of coping behavior will affect the patients' long-term outcome and treatment will maintain more lasting effects on functioning.

The present study offers empirical evidence for the implementation of psychological interventions in an early stage of the disease to possibly prevent an unfavorable long-term outcome in rheumatoid arthritis patients. Shortly after diagnosis, it was possible to identify psychosocial risk factors, such as the frequent use of passive pain coping strategies and a smaller social network, for a deterioration in functional status within one year, probably indicating the early manifestation of avoidance mechanisms in the face of a chronic stressor.

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3

3.1 Coping and Social Support

3.1.2 Predictors of functional disability and pain

3.1.2.2 Pain coping and social support as predictors of long-term functional disability and pain in early rheumatoid arthritis

Evers, A.W.M., Kraaimaat, F.W., Geenen, R., Jacobs, J.W.G. & Bijlsma, J.W.J. (2003). Pain coping and social support as predictors of long-term functional disability and pain in early rheumatoid arthritis. *Behaviour Research and Therapy (in press).*

ABSTRACT

Pain-related avoidance factors and social resources, as assessed by pain coping and social support, are supposed to have lasting effects on functional disability and pain in chronic pain disorders. As a follow-up to a prospective study demonstrating short-term effects after one year (Evers et al., 1998a), the role of pain coping and social support at the time of diagnosis was investigated in relationship to the long-term course of functional disability and pain after 3 and 5 years in 78 patients with rheumatoid arthritis (RA), taking into account personality characteristics of neuroticism and extraversion, clinical status and use of medication. In line with findings at the 1-year follow-up, results showed that more passive pain coping predicted functional disability at the 3-year, but not the 5-year follow-up. In addition, low levels of social support at the time of diagnosis consistently predicted both functional disability and pain at the 3 and 5-year follow-ups. Results indicate that pain coping and social support, assessed very early in the disease process, can affect long-term functional disability and pain in RA, and suggest that early interventions focusing on pain-related avoidance factors and social resources for patients at risk may beneficially influence long-term outcomes in RA.

INTRODUCTION

Rheumatoid arthritis (RA), a chronic inflammatory disease affecting the joints, is one of the most costly musculoskeletal disorders, primarily due to the impairment of daily activities and loss of work as a consequence of functional disability and pain (Allaire et al., 1994; Yelin & Callahan, 1995). In the first year of the disease, impaired functioning and elevated pain levels are already comparable to that of patients with longstanding RA (Meenan et al., 1991; Evers et al., 1997, 1998a), about 40% of the patients face occupational disability, and 75% suffer from limitations affecting their leisure time and social activities (Fex et al., 1998; van Jaarsveld et al., 1998; Albers et al., 1999). In addition, functional impairment in the first year of RA predicts future loss of employment, a worse long-term prognosis and mortality (Sherer et al., 1986; Rasker & Cosh, 1989; Corbett et al., 1993; Eberhardt et al., 1993; Fex et al., 1998). Consequently, medical treatment is increasingly geared toward more aggressive treatment in the initial stage of the disease to decrease unfavorable long-term disease outcomes (van de Putte et al., 1998; van Jaarsveld et al., 2000).

Irrespective of the influence of biomedical factors, chronic pain research has supplied relatively convincing evidence that psychosocial factors can affect the course of functional disability and pain in patients with RA and other chronic pain disorders (see for reviews e.g., Linton, 2000; Keefe et al., 2002; Turk & Okifuji, 2002). Specifically, fear-avoidance models have received wide attention and provided supportive evidence that pain-related avoidance factors, such as avoiding activity and catastrohpic pain cognitions, are linked to future pain outcomes in chronic pain patients (e.g., Lethem et al., 1983; Linton, 1985; Philips, 1987; Vlaeyen et al., 1995; Vlaeyen & Linton, 2000). Fear-avoidance and the associated avoidance of activity are supposed to result in enhanced physical impairment, e.g. due to physical deconditioning processes, decreased muscular endurance and strength. Cognitive responses consisting of fearful, catastrophizing beliefs about pain are thought to bring about a preoccupation with bodily symptoms and avoidance of activity, which in turn exacerbate pain and functional disability. Besides cognitive-behavioral factors, social resources are assumed to have an impact on long-term chronic pain outcomes, including social networks and perceived support from close others, which may inhibit avoidance of physical and social activities, and have a beneficial impact on functional disability and pain (e.g., Cohen & Wills, 1985; Uchino et al., 1996; Keefe et al., 2002).

In addition to experimental and cross-sectional research, prospective studies have demonstrated the relevance of pain-related avoidance factors and social resources in various chronic pain populations, including RA patients (see e.g., Jensen et al., 1991b; Linton, 2000; Keefe et al., 2002; Turk & Okofuji, 2002). For example, in one of the first prospective studies conducted by Brown and Nicassio (1987), passive coping with pain, including the restriction of activities and

catastrophic pain cognitions, predicted functional disability and pain in RA patients after 6 months. Behavioral and cognitive factors also independently predicted future RA outcomes: avoidance of activity was related to increased functional disability after 1 year (Evers et al., 1998a; van Lankveld et al., 1998), while worrying and catastrophic pain cognitions predicted functional disability and pain after 6 months (Keefe et al., 1989) and functional disability after 1 year (Evers et al., 1998b). In contrast, active coping with pain by ignoring pain sensations, using distraction or continuing activities in spite of pain have only incidentally been linked to more favorable future outcomes (e.g., Brown & Nicassio, 1987), suggesting that not using passive coping strategies may be more crucial than the use of specific active strategies (see e.g., Jensen et al., 1991b; Turk & Rudy, 1992). Apart from pain coping, there is also increasing evidence that social support, such as qualitative aspects of perceived social support and quantitative aspects of the size of social networks, affect future functional limitations and pain in chronic pain patients. For example, lower levels of perceived support have been shown to be prospectively related to more interference in daily activities in RA patients after 1 year (Smith & Wallston, 1992) and increased pain after 1 year (Waltz et al., 1998), while less extended social networks predicted functional disability after 1 year (Evers et al., 1998a).

In view of the empirical evidence on RA and comparable findings in other chronic pain disorders (see e.g., Jensen et al., 1991b; Linton, 2000; Keefe et al., 2002), there seems to be relatively clear support that pain coping and social resources affect future outcomes in chronic pain patients. However, prospective studies among RA and other chronic pain patients have generally assessed the impact of these factors on future outcomes over a relatively short period of time (no longer than 1 year), which can be considered rather short-term outcomes in the realm of chronic conditions. Fear-avoidance models usually propose that once avoidance mechanisms have been established they result in increasing detrimental effects over time and affect long-term outcomes (Lethem et al., 1983; Philips, 1987; Vlaeyen et al., 1995). However, relevant variables could differ for short-term and long-term outcomes. For example, solely the combination of cognitive-behavioral and social factors - and not single factors - could have an impact on long-term outcomes, e.g. for patients with more passive pain coping and less social support. In addition, personality characteristics and biomedical factors may have long-term modifying effects. For example, the personality characteristics of neuroticism and extraversion and patients' clinical status have been shown to possibly modify the relationship of pain coping and social resources to outcomes in chronic pain patients, suggesting that the detrimental effects of passive pain coping or fewer social resources might only occur in patients with more neuroticism, less extraversion and a worse clinical status (e.g. Brown et al., 1989b; Wade et al., 1992; Vlaeyen et al., 1999; Phillips & Gatchel, 2000). Finally, pain coping and social resources have been shown to affect first year outcomes (Evers et al.,

1998a), and correspondence with findings for longstanding RA suggests that the same mechanisms are involved both early in the disease and later on. Since pain coping and social resources may be a focus of early intervention, it is particularly relevant to show whether these factors affect long-term functional disability and pain in RA patients at the earliest point in time for intervention - at diagnosis.

The object of the present study was to examine the long-term effects of pain coping and social support on functional disability and pain in patients with early RA. This study was conducted as a follow-up to the previously reported effects of pain coping and social support (Evers et al., 1998a), showing that passive pain coping strategies, and to a lesser degree lower levels of social support, assessed at the time of diagnosis, predicted the course of functional disability in the first year. Additional analyses revealed that these factors did not predict the 1-year pain outcome in this sample. Our current study aims at follow-up results, studying the effects of active and passive pain coping and social support at the time of diagnosis on the course of functional disability and pain after 3 and 5 years. In line with the literature supporting short-term effects, less active and more passive pain coping and lower levels of social support were expected to predict a less favorable long-term course of functional disability and pain. In addition to these main effects, it was examined whether the personality characteristics of neuroticism and extraversion account for the relationship between pain coping, social support and the long-term outcome. The possible moderator effects of personality characteristics and clinical status on pain coping and social support were also explored, assuming that the effects of less active and more passive pain coping and lower levels of social support on functional disability and pain would be greater in patients with personality characteristics of more neuroticism and less extraversion and in patients with a worse clinical status at the time of diagnosis. Finally, the moderator effects of social support on pain coping were exploratively examined, predicting that the detrimental effects of less active and more passive pain coping are increased in patients with lower levels of social support.

METHODS

Sample and Procedure

The sample consisted of outpatients with recently diagnosed RA from five hospitals in the Netherlands. All patients participated in one of two medical trials for second-line anti-rheumatic drugs (van Jaarsveld et al., 2000; van Everdingen et al., 2002). Inclusion criteria for the trials were a minimum age of 18 years, diagnosis according to the 1987 American College of Rheumatology (ACR) criteria (Arnett et al., 1988), and a duration of disease of less than one year. Exclusion criteria were comorbid conditions that might interfere with one of the

medication strategies (such as malignancy, cardiac, respiratory, hepatic, and renal insufficiency), previous or current treatment with second-line anti-rheumatic drugs, glucocorticoids, cytotoxic or immunosuppressive drugs, possible pregnancy or breast feeding, and psychiatric or mental disturbances that severely interfere with adherence to the study protocol. Patients were informed about this study by their rheumatologists when ACR criteria were assessed. About three weeks later (range 0 - 12 weeks), clinical and self-report data were assessed during their following visit. This visit was also the starting point for the prospective medical trials. Five patients did not return the questionnaires at this assessment point, resulting in the participation of 95 patients in the present study at the time of diagnosis. In addition to assessing clinical and self-report data at the beginning of the study and at the 1-year follow-up (Evers et al., 1998a), data on disease activity, functional disability, and pain was again collected at the 3 and 5-year follow-ups.

Of the 95 patients who correctly completed self-report data at the first assessment, 78 patients (82%) completed all assessment points during the 5-year study period. In terms of dropouts, 7 patients died, 2 moved, 1 was in remission and no longer treated by the rheumatology outpatient clinic and 7 did not complete the questionnaires for the follow-up assessments. When entering the study, dropouts did not significantly differ from participants in terms of demographic variables (sex, age, marital status, educational level), disease activity, functional disability, pain, the personality characteristic of extraversion, pain coping or social support. However, dropouts scored higher on the personality characteristic of neuroticism than patients who completed all assessment points ($t = 2.87$, $p < 0.01$).

Of the 78 participants in the follow-up, 69% were female, 76% married or living with a partner, and 32% and 57% had a primary or secondary educational level, respectively. Mean age at the time of entering the study was 57 years (range 20 - 82 years). The distribution of medication strategies was as follows: 30% and 23% of the patients used non-steroidal anti-inflammatory drugs (NSAID) alone at first assessment and at the 5-year follow-up, respectively; the other patients took NSAID in combination with methotrexate (30% and 49%, respectively), intramuscular gold (14% at both assessment points), hydroxychloroquine (15% and 9%, respectively), prednisone (11% and 1%, respectively) or other second-line medication, prescribed only for individual patients (4% at the 5-year follow-up). At the 5-year follow-up, 31% of the patients still used the initially prescribed medication, 65% used another medication strategy from the drug trial, and 4% of the patients used another second-line medication than that used in the medication trials.

Measures

Demographic variables were assessed with a general checklist, assessing patient gender, age, marital status and educational level. Educational level was measured with 7 categories that can be classified as primary, secondary and tertiary educational levels, representing an average of 7, 12, and 17 years of education, respectively.

Disease activity was determined by erythrocyte sedimentation rate (ESR; 1-140mm first hour), an indicator of inflammatory activity, and by joint score ratings of the simultaneous presence of swelling and tenderness in 38 joints (range 0-534) (Thompson et al., 1987). A composite score of both measures was used as an indicator of disease activity, in accordance with regular use of composite scores of disease activity that consist of at least ESR or another acute phase reactant and a joint score (van der Heijde et al., 1992; Prevoo et al., 1995). The composite score was calculated by adding the standardized scores (*z*-scores) of both indicators. A higher composite score indicates higher levels of disease activity.

Functional disability was assessed using a composite score of one clinical measure and two self-report measures (see Evers et al., 1998a). The clinical measure consisted of grip strength assessments with a Martin vigorimeter (the mean of three measurements on both hands was calculated). Self-reported functional disability was assessed with the Mobility and Self-care scales of the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL; Huiskes et al., 1990a; Evers et al., 1998b). The IRGL is derived from the Arthritits Impact Measurement Scales (AIMS) and assesses physical, psychological and social health in patients with rheumatic diseases. Previous research has shown that the reliability and validity of the IRGL scales are highly satisfactory (Huiskes et al., 1990a; Evers et al., 1998b). Items in the IRGL scales are scored on a 4-point or 5-point Likert scale. The Mobility and Self-care scales assess the functional capacities of the lower and upper extremities, respectively, over the last month (15 items). Cronbach's alpha in the present study was 0.89 for both scales. A composite score of the clinical measure and the two self-report scales was calculated by adding the standardized scores (*z*-scores) of all three indicators. A higher composite score indicates higher levels of functional disability.

Pain was assessed with the IRGL Pain scale (6 items), measuring the severity and frequency of painful episodes and swollen joints and the duration of early morning stiffness in the last month. Cronbach's alpha in the present study was 0.88.

Personality dimensions, i.e. neuroticism and extraversion, were measured with a Dutch version of the Eysenck Personality Questionnaire (17 and 12 items, respectively) (EPQ; Wilde, 1970; Eysenck & Eysenck, 1991). Cronbach's alphas in the present study were 0.90 for neuroticism and 0.79 for extraversion.

Pain coping was assessed by the Pain Coping Inventory (PCI; Kraaimaat et al., 1997; Kraaimaat & Evers, 2003), measuring active and passive coping strategies

when dealing with pain. Active pain coping strategies reflect three cognitive-behavioral strategies, measuring patients' efforts to distract themselves from the pain (Distraction, 5 items), to reinterpret and transform the pain (Pain Transformation, 4 items) and to function in spite of the pain (Reducing Demands, 3 items). Passive pain coping reflects three cognitive-behavioral strategies, assessing behavioral tendencies to restrict functioning (Resting, 5 items), to avoid environmental stimuli (Retreating, 7 items) and catastrophic cognitions about the pain (Worrying, 9 items). A composite score of active and passive pain coping can be calculated by summing up the nonweighted scores of the three active and passive coping strategies (Kraaimaat et al., 1997; Kraaimaat & Evers, 2003). Cronbach's alpha for the active and passive scales were 0.79 and 0.90, respectively, in the present study.

Social support in the past six months was measured with the IRGL social functioning scales, reflecting a quantitative and qualitative aspect of social support. The quantitative aspect was assessed by the size of the social network, i.e. the number of friends and family members with whom patients associate. The qualitative aspect was measured by the Perceived Support scale (5 items), inquiring about the perceived availability of emotional and instrumental support (availability to share sad and pleasant events, obtain support when faced with stress and pain, get help for casual work). Cronbach's alpha for the Perceived Support scale in the present study was 0.88.

Statistical Analyses

Mean linear changes in clinical status (disease activity, functional disability, pain) were studied by analyses of variance with repeated measurements, using the variables at the different assessment points as dependent variables, followed by posthoc tests in the event of significant linear changes. To explore the relationship between predictors at the time of diagnosis and changes in functional disability and pain after 3 and 5 years, Pearson correlation coefficients were calculated between the predictors at the time of diagnosis and the residual gain scores for functional disability and pain at the 3 and 5-year follow-ups (Kerlinger, 1975). Sequential regression analyses were then performed to examine the relative contribution of predictors on functional disability and pain at the 3 and 5-year follow-ups. Functional disability and pain at the 3 and 5-year follow-ups were used as dependent variables. In the first step, the baseline assessment of the dependent variable was entered, followed by the predictors significantly related to change in functional disability or pain at at least one follow-up assessment. Mediating effects were determined with the procedure described by Baron and Kenny (1986). Moderating effects were explored by calculating centered interaction terms between the predictor and the moderator and entering them in the regression analyses, after controlling for their main effects. Due to the relatively high number of explorative tests performed in these moderator analyses, a more conservative

threshold of $p < 0.01$ was used. Finally, to control for possible confounding effects of medication, Pearson correlation coefficients were calculated between the use (use vs. nonuse) and duration (number of years) of every medication strategy separately and the residual gain scores of functional disability and pain at the 3 and 5-year follow-ups. In the event of a significant correlation, the effects of the medication strategy were taken into account by entering the medication strategy at step 2, before the other predictors in the regression analyses.

RESULTS

Change in Clinical Status during the Study Period

During the 5-year period, there was a significant mean decrease in disease activity ($F(3,73) = 22.2$, $p < 0.001$ and $F(3,73) = 10.6$, $p < 0.01$ for the ESR and joint score, respectively). In addition, pain and one indicator of functional disability significantly decreased within 5 years after diagnosis ($F(3,75) = 9.6$, $p < 0.01$ for pain; $F(3,75) = 14.5$, $p < 0.001$ for grip strength). Posthoc tests indicated that this improvement in clinical status was most obvious in the first year of the disease: all indicators markedly decreased in this year ($t = 3.06$, $p < 0.01$ for ESR; $t = 3.25$, $p < 0.01$ for the joint score; $t = 2.20$, $p < 0.05$ for pain; $t = 4.29$, $p < 0.001$ for grip strength; see also Evers et al., 1998b), possibly due to the beneficial effects of medication (van Jaarsveld et al., 2000; van Everdingen et al., 2002). After the first year of the disease, clinical status remained relatively stable, as indicated by nonsignificant posthoc tests between 1 and 3 and between 3 and 5 years, with one exception: an indicator of disease activity, ESR, significantly decreased further between the 1 and 3-year follow-ups ($t = 3.11$, $p < 0.01$).

Predictors of Functional Disability at the 3 and 5-Year Follow-ups

The results of the correlational analyses between predictors at the time of diagnosis and change in functional disability are presented in Table 1. The use of more passive pain coping strategies at the time of diagnosis was significantly related to an increase in functional disability after 3 years, but not after 5 years. In addition, both indicators of social support, perceived support and social networks were significantly related to less increase in functional disability at the 3 and the 5-year follow-ups. No significant relationships were found between demographic variables, the personality characteristics of neuroticism and extraversion, disease activity, pain and active pain coping at the time of diagnosis and changes in functional disability at the 3 and 5-year follow-ups.

Sequential regression analyses were then conducted with the predictors significantly related to the change in functional disability at at least one assessment point: passive pain coping and both indicators of social support. After controlling

for baseline levels of functional disability at the first step, passive pain coping and social support indicators assessed at the time of diagnosis were entered in the following steps. As demonstrated in Table 2, passive pain coping significantly contributed 4% to functional disability at the 3-year follow-up, but did not significantly add variance to functional disability at the 5-year follow-up. In addition, lower levels of social support explained 12% and 11% additional variance in functional disability at the 3 and 5-year follow-ups, respectively. Standardized beta coefficients indicated that passive coping with pain, lower levels of perceived support and a smaller social network at the time of diagnosis all significantly predicted functional disability at the 3-year follow-up ($t = 2.49$, $p < 0.05$; $t = -2.20$, $p < 0.05$; $t = -2.98$, $p < 0.01$, respectively). Lower levels of perceived support and a less extended social network also predicted functional disability at the 5-year follow-up ($t = -2.70$, $p < 0.01$; $t = -2.07$, $p < 0.05$, respectively).

Table 1 Correlations between Predictors at the Time of Diagnosis and Changes in Functional Disability and Pain after 3 and 5 Years in 78 RA Patients [a]

	Change in functional disability		Change in pain	
	3 yrs.	5 yrs.	3 yrs.	5 yrs.
Demographic variables				
Age	-.03	.07	-.10	.09
Sex	.16	.09	.06	.04
Educational level	.01	-.16	-.02	-.31**
Marital status	-.11	-.04	-.11	.15
Personality characteristics				
Neuroticism	.21	.21	.15	.11
Extraversion	-.17	-.04	.02	.14
Clinical status				
Disease activity	.09	.19	.17	.10
Functional disability	-	-	.27*	.26*
Pain	.13	.11	-	-
Pain coping				
Active	-.17	.00	-.18	-.10
Passive	.24*	.19	.20	.10
Social support				
Perceived support	-.30**	-.34**	-.26*	-.28*
Social network	-.36**	-.29*	-.13	-.14

[a] A positive correlation indicates that the predictor is related to an increase in functional disability and pain (residual gain scores).
* $p < 0.05$ ** $p < 0.01$.

To study whether the relationship between passive pain coping and increased functional disability at the 3 and 5-year follow-ups was mediated by social support, the order of entering passive pain coping and social support was reversed, revealing overall the same results. Passive pain coping at step 3 still significantly predicted functional disability at the 3-year follow-up but not at the 5 year follow-up, after controlling for social support at step 2, indicating that passive pain coping was an independent predictor of functional disability.

Analyses of the moderator effects of personality characteristics and clinical status on pain coping and social support and of pain coping on social support indicated that the interaction terms were not significantly related to changes in functional disability at the 3 and 5-year follow-ups, failing to support any moderating function of the predictors for changes in long-term functional disability.

Table 2 Multiple Regression Analyses Predicting Functional Disability at the 3 and 5-Year Follow-ups from Predictors at the Time of Diagnosis [a]

	Functional disability after 3 yrs.		Functional disability after 5 yrs.	
	ß	Δ R^2	ß	Δ R^2
Functional disability	.52***	.37***	.51***	.34***
Pain coping		.04*		.03
Passive	.21*		.17	
Social support		.12***		.11**
Perceived support	-.18*		-.24**	
Social network	-.25**		-.18*	
Total Δ R^2		.53***		.48***

[a] Selection criterion for predictor variables was a significant correlation with changes in functional disability at least at a single follow-up assessment (see Table 1).
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$.

Predictors of Pain at the 3 and 5-Year Follow-ups

As presented in Table 1, correlational analyses between predictors at the time of diagnosis and changes in pain after 3 and 5 years revealed a significant relationship between lower educational level and an increase in pain at the 5-year follow-up, but not at the 3-year follow-up. In addition, higher levels of functional disability and lower levels of perceived support at the time of diagnosis were related to an increase in pain at the 3 and 5-year follow ups. In contrast, demographic variables (sex, age, marital status), the personality characteristics of neuroticism and extraversion, active and passive pain coping, and the size of the

social network were not significantly related to changes in pain at the 3 and 5-year follow-ups.

When entering the predictors significantly related to changes in pain at at least one assessment point in sequential regression analyses, i.e. educational level, functional disability, perceived support, results indicated that perceived support significantly explained an additional 5% variance in pain at both assessment points, after controlling for baseline levels of pain, educational level and functional disability at the time of diagnosis (see Table 3). Standardized beta coefficients indicated that lower levels of perceived support at the time of diagnosis significantly predicted an increase in pain at the 3 and 5-year follow-ups (t = -2.34, $p < 0.05$ and t = -2.43, $p < 0.05$, respectively).

Finally, analyses of the moderator effects of personality characteristics and clinical status on pain coping and social support and of pain coping on social support were performed, indicating nonsignificant correlations between all interaction terms and changes in pain at the 3 and 5-year follow-ups, failing to support any moderating function of the predictors for changes in long-term pain.

Table 3 Multiple Regression Analyses Predicting Pain at the 3 and 5-Year Follow-ups From Predictors at the Time of Diagnosis [a]

	Pain after 3 yrs.		Pain after 5 yrs.	
	ß	Δ R^2	ß	Δ R^2
Pain	.36**	.17***	.44***	.20***
Demographic variables		.00		.08**
Educational level	.03		-.25*	
Clinical status		.06*		.04
Functional disability	.25*		.19	
Social support		.05*		.05*
Perceived support	-.23*		-.23*	
Total Δ R^2		.28***		.37***

[a] Selection criterion for predictor variables was a significant correlation with changes in functional disability at least at a single follow-up assessment (see Table 1).
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$.

Confounding Effects of Medication

Correlation coefficients between the use (use/nonuse) and duration (number of years) of the different medication strategies and changes in functional disability and pain at the 3 and 5-year follow-ups indicated nonsignificant correlations between all strategies and changes in long-term functional disability and pain, with

one exception: the use and duration of taking NSAID was related to a decrease in functional disability at the 3 year follow-up ($r = 0.25$, $p < 0.05$ and $r = 0.24$, $p < 0.05$, respectively), but not at the 5-year follow-up. However, when controlling for this medication strategy in the regression analyses by entering it at step 2 (see Table 2), passive pain coping and social support still significantly predicted functional disability at the 3-year follow-up. In addition, standardized beta coefficients showed the same significant predictors as previously found, i.e. passive pain coping and both indicators of social support (see Table 2), indicating that their effects could not be ascribed to the medication usage.

DISCUSSION

The role of pain coping and social support was examined in relationship to the long-term outcome of functional disability and pain in early RA. In line with previous results at the 1-year follow-up (Evers et al., 1998a), passive pain coping assessed at the time of diagnosis still had a detrimental effect on functional disability at the 3-year follow-up, but not at the 5-year follow-up. In addition, social support consistently predicted a less unfavorable course of functional disability and pain at the 3 and 5-year follow-ups, and these effects occurred irrespective of the personality characteristics of neuroticism and extraversion, clinical status and use of medication, generally suggesting that pain-related avoidance factors and social resources have a lasting impact on physical outcomes in early RA.

In patients with chronic pain, particularly RA, several studies supported the unfavorable effects of avoidance of activities and negative pain cognitions on future functional disability (Brown & Nicassio, 1987; Keefe et al., 1989; Smith & Wallston, 1992; van Lankveld et al., 1998, see also Jensen et al., 1991; Linton, 2000; Vlaeyen & Linton, 2000; Turk & Okofuji, 2002). In line with these studies, assessing relatively short periods of time of a maximum of 1 year, our present study suggests that these effects are more long lasting than previously assessed. Passive pain coping, consisting of worrying cognitions about pain and the behavioral strategies of resting and retreating, assessed at the time of diagnosis still affected functional disability 3 years after diagnosis. Posthoc analyses indicated that these effects could be largely ascribed to the behavioral component of avoidance of activity. When analyzing the different contribution of the two behavioral and the cognitive scales to future functional disability, only resting significantly predicted additional variance in functional disability at the 3-year follow-up ($p < 0.01$). Worrying also tended to be related to functional disability at the 3-year follow-up, but its effect was nonsignificant in regression analyses. While resting and worrying both significantly contributed to short-term functional disability after one year (Evers et al., 1998a), the behavioral component of

avoidance of activity appeared to be most crucial for more longlasting effects on functional disability. These findings may support the assumption of fear-avoidance models that the most direct links to long-term functional disability are physiological disuse processes of deconditioning and reduced muscle strength and coordination (see e.g., Bortz, 1984; Vlaeyen & Linton, 2000; Steultjens et al., 2002).

In contrast to expectations, passive pain coping did not predict long-term pain in this sample of patients with early RA. In fact, cognitive and behavioral pain coping strategies have been shown to predict future disability more consistently than future pain in chronic pain patients (see e.g., Evers et al., 2001b), and as far as we know there are only two prospective studies that have found detrimental effects for passive pain coping or catastrophizing on future pain in RA patients (Brown & Nicassio, 1987; Keefe et al., 1989). These studies were conducted with much larger sample sizes and a lack of power may be one reason for nonsignificant effects in the present study. In addition to cognitive-behavioral factors, our own research in longstanding RA indicated that self-reported physiological reactivity to pain was a better predictor than cognitive or behavioral pain coping for pain after 1 year (Evers et al., 2001b), suggesting that symptom-specific patterns of physiological pain reactivity or physiological fear reactions to pain may be more directly linked to changes in pain than cognitive and behavioral pathways (see e.g., Flor et al, 1990; Turk & Flor, 1999). Aside from physiological factors, possible cognitive mediators not assessed in the present study have been shown to be relevant in the relationship to functional disability and pain in chronic pain patients, such as pain-related fears, heightened attention to bodily symptoms due to hypervigilance or expectations of increased pain (see e.g., Vlaeyen & Linton, 2000), and these factors may also be crucial for long-term functional disability and pain in this sample of patients with early RA.

Irrespective of pain coping, social support predicted long-term functional disability and pain in this sample of patients with early RA. Specifically, both indicators of social support, perceived support and the size of the social network, significantly predicted a less unfavorable long-term course of functional disability after 3 and 5 years. In comparison to the short-term follow-up after 1 year when only the size of the social network had a slight effect on future functional disability (Evers et al., 1998a), both indicators of social support were relatively strongly related to functional disability at the 3 and 5-year follow-ups. In addition, in contrast to the nonsignificant effects of all predictors for pain at the 1-year follow-up, lower levels of perceived support also consistently predicted pain at the 3 and 5-year follow-ups, generally indicating that the effects of social support particularly affect the long-term outcome of functional disability and pain in RA. These effects seem to supplement findings in the RA literature, showing that a lack of social support is prospectively related to greater interference in daily life after 1 year (Smith & Wallston, 1992) and to more pain after 1 year (Waltz et al., 1998).

Questions arise about possible cognitive-behavioral or physiological mediators in the relationship between social support and long-term outcomes. From a cognitive-behavioral perspective, perceived support from significant others has been shown to be linked to less pain behaviors and greater activity levels in heterogeneous groups of chronic pain patients (Jamison & Virts, 1990), as well as to more information seeking and cognitive restructuring in RA patients (Manne & Zautra, 1989). The latter study also revealed a path model, in which perceived support leads to more adaptive coping which in turn predicted better adjustment in RA patients (Manne & Zautra, 1989), suggesting that social support may figure as coping assistance (Thoits, 1986) and result in more adaptive pain coping and less withdrawal from (social) activities, which beneficially affect long-term functional disability and pain. Similar mechanisms may be responsible for the favorable effects of a larger social network on long-term functional disability in the present sample, e.g. stimulating participation in social activities, inhibiting avoidance behavior and offering coping assistance by generating multiple solutions to problems. Apart from cognitive-behavioral pathways, physiological mediators in the relationship between social support and physical health have frequently been reported (see e.g., Uchino et al., 1996), and altered autonomic and muscular reactivity or immunological function may be responsible for the favorable effects of social support on long-term outcomes. A major challenge for future research is to link various social support components to specific cognitive, behavioral and physiological pathways in their relationship to patient long-term functioning

What might be the implications of our results with respect to fear-avoidance models for RA and other chronic pain patients? In line with assumptions of fear-avoidance models (e.g., Lethem et al., 1983; Philips, 1987; Vlaeyen et al., 1995), our study indicates that pain-related avoidance factors and social resources can have a lasting impact on patient functioning. In addition, these factors appear to be established at a very early stage of the disease, i.e. at the time of diagnosis, suggesting that they result from the patients' prior learning history, pre-dispositional factors and/or cultural backgrounds (see e.g., Philips, 1987; Turk & Flor, 1999; Turk & Okofuji, 2002). Moreover, our results suggest that the relative contribution of pain-related avoidance factors and social resources change between short and long-term outcomes. The cognitive aspects of worrying and behavioral aspects of avoidance of activity seem to be especially relevant for short-term functional disability, with the behavioral component of avoidance of activity having a continuing effects on longer-term follow-ups. In contrast, social support appears to have initially only marginal effects, but its influence increases on long-term functional disability and pain outcomes, suggesting that the role of social resources may have been largely underestimated in chronic pain research.

Some limitations of this study have to be considered. Our sample consisted of patients with early RA, for whom pharmacological treatment appeared to have beneficial effects (van Jaarsveld et al., 2000; van Everdingen et al., 2002).

Although our results correspond to findings for other chronic pain disorders, the extent to which our results can be generalized to other chronic pain patients or patients with longstanding RA is unclear. Our results may be also influenced by some selection bias, since all patients participated in a clinical trial and dropouts scored somewhat higher on neuroticism than participants. The relatively general assessment of passive pain coping and social support in our study limits the possibility of drawing conclusions about specific pathways for how these factors may affect long-term functional disability and pain in early RA, and it remains unclear to what extent they are a consequence of fear-avoidance beliefs or hypervigilance, as suggested by fear-avoidance theories (see e.g. Vlaeyen & Linton, 2000), or other more depressogenic cognitive processes, such as helplessness (Evers et al., 2001a). In addition to these cognitive pathways, future studies should include an examination of behavioral pathways, such as observed or self-monitored activity assessments (e.g., Linton, 1985), physiological pathways, such as physiological pain reactivity, generalized fear reactions and measures of muscle strength (Flor et al., 1990; Vlaeyen et al., 1999; Evers et al., 2001b; Steultjens et al., 2002), as well as social pathways, including observed supportive and problematic indicators of social responses to pain (e.g., Flor et al., 1987; Manne & Zautra, 1989). Finally, multiple repeated measurements of pain coping, social support, pain and functional disability are needed to gain insight into possible reciprocal effects, in which pain-related avoidance factors, a lack of social resources and poorer physical functioning might enhance each other during the course of disease

For clinical practice, tailored cognitive-behavioral treatment at an early stage of the disease, aimed at decreasing pain-related avoidance factors and increasing social resources in RA patients at risk, has recently been shown effective in producing beneficial changes in physical and psychological functioning at post-treatment and follow-up (Evers et al., 2002b). Results of the present study suggest that this kind of tailored treatment for patients at risk not only induce short-term changes, but might also lastingly modify long-term functioning, particularly when systematically promoting patients' social support systems.

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3

3.1 Coping and Social Support

3.1.3 Predictors of psychological distress

3.1.3.1 Determinants of psychological distress and its course in the first year after diagnosis in rheumatoid arthritis patients

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ABSTRACT

In order to examine determinants of psychological distress and its course in the first year after diagnosis in rheumatoid arthritis patients, self-report data and clinical and laboratory measures were collected in 91 patients (70% female, mean age 57 years) shortly after diagnosis and one year later. Multiple regression analysis indicated that sex, pain and functional status, disease impact on daily life, life events, and perceived social support were related to psychological distress (anxiety and depressed mood) shortly after diagnosis. Coping strategies were related to distress levels only one year later. Multiple regression analysis of change in anxiety and depressed mood revealed that a decrease of psychological distress after one year could be predicted by male sex, an initially less severe inflammatory activity and an initially more extended social network. In addition, a decrease in distress was related to parallel improvements in clinical status. Results indicate the importance of a multimodal assessment of demographic variables, clinical and life stressors and social resources for the understanding of distress and the identification of risk factors in the first stage of the disease. Personal coping resources appear to become more important predictors of distress in a later phase of the disease.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, unpredictive and progressive inflammatory disease primarily affecting the joints. After diagnosis, the patient is confronted with a new, unexpected, and uncontrollable stressor with actual as well as foreseeable long-term consequences in physical, psychological, and social areas of life. Physical disability, pain, social dependency, uncertainty about disease progression, and threats to one's self-esteem are some of the consequences of the disease that impose great demands on the patient's adaptive capabilities and may increase psychological distress.

Raised levels of anxiety and depressive symptoms have frequently been reported and are indicative of a prevalence of about 20% in patients with longstanding RA (e.g., Bishop et al., 1987; Frank et al., 1988; Murphy et al., 1988; Katz & Yelin, 1993). Whether the psychological status of recently diagnosed patients is different to that of patients with longstanding RA is not yet clear. It has been supposed that an increased level of psychological distress would be expected shortly after the diagnosis as a reaction to a personally threatening event, with an ensuring process of psychological adjustment to the disease, due to a growing capacity to cope with the stressor later on (Newman et al., 1989; Devins et al., 1992). Shorter illness duration has been shown to be related to increased levels of depression by Deyo et al. (1982), Newman et al. (1989), Katz and Yelin (1993), Wolfe and Hawley (1993) and Chaney et al. (1996), while Meenan et al. (1991) reported no differences between recently diagnosed patients (disease duration of less than one year) and those with more established disease. Little is known about the factors which affect psychological status shortly after the diagnosis and which predict its course in the first stage of the disease. The relative amount of psychological distress as well as the process of adaptation to a chronic disease are supposed to be both affected by the encountered stressors and the resources available (Lazarus & Folkman, 1984).

Research in RA patients with established disease has indicated that a broad set of physical, psychological, and social stressors and resources are relevant for the understanding and prognosis of psychological distress. The disease itself and the clinical status figure as important stressors in RA patients. Especially pain and the patient's functional status have been shown to be related to depression in recently diagnosed patients (disease duration of less than one year) (van der Heide et al., 1994a), in patients with more established disease (mean disease duration of three years) (Brown, 1990; Nicassio & Wallston, 1992) and in patients with longstanding RA (mean disease duration of more than ten years) (Newman et al., 1989; Wolfe & Hawley, 1993). Less evidence has been found with regard to a relation between distress and clinical measures such as blood sedimentation rate and joint score (e.g. Newman et al., 1989; Bijlsma et al., 1991; Wolfe & Hawley, 1993). In addition, there is suggestive evidence that the impact of the disease on

daily life, such as the impact on household activities, income, work, sexuality and leisure activities, figures as an important stressor affecting psychological distress in patients with longstanding RA. Indicative of a positive relationship between disease impact on daily life and depressed mood are the results of Devins et al. (1992), Brons et al. (1993) and Katz and Yelin (1995). Finally, stress research has focused on the occurrences of major life events. Studies in patients with longstanding RA yielded equivocal results, and significant relations between major events and health outcomes in RA patients were rather low (e.g., Rimon & Laakso, 1985; Klages, 1991; Brons et al., 1993; Koehler & Vertheim, 1993).

Individual differences in psychological distress independent from health status suggest that various psychological processes, such as receiving social support and the way of coping with stressors, mediate or modify the relationship between stressors and the psychological reaction to a chronic disease (Lazarus & Folkman, 1984; Cohen & Wills, 1985). One main conceptualization of social support is the distinction between qualitative aspects, such as the perceived availability of support, and quantitative aspects, such as the size of the social network (Cohen & Wills, 1985). In accordance with Cohen and Wills (1985), research suggested that qualitative aspects of social support are more important than quantitative aspects in patients with a disease duration of about three years (Brown et al., 1989b) and in patients with longstanding RA (Goodenow et al., 1990). From investigations of coping strategies among individuals with RA, it can be concluded that passive, avoidant and emotion-focused ways of coping are related to maladaptive functioning, whereas active and problem-focused coping strategies are associated with adaptive functioning (for review, see Manne & Zautra, 1992; Young, 1992).

The multimodal influence of these determinants on psychological distress shortly after diagnosis and its course in the first year of the disease have not yet been investigated in RA patients. The stressors and coping resources might be partly different for recently diagnosed patients which are relatively inexperienced with a chronic stressor. In order to gain insight into predictors of psychological distress and its course in the first year of the disease, we examined the extent to which demographic variables, clinical status, disease impact, life events, social support, and coping strategies shortly after diagnosis predict the level of psychological distress and its course in the first year after diagnosis. We expected that a high level of distress shortly after diagnosis as well as a smaller decrease in psychological distress within the first year of the disease would be related to an initially worse clinical status, a greater amount of disease impact on daily life, the occurrence of more life events, and less personal and social coping resources.

METHODS

Patients

The sample consisted of successive outpatients with recently diagnosed RA from five hospitals in the Utrecht area, the Netherlands. Patients were participating in a prospective study on the effects of different medication strategies. Inclusion criteria were a minimum age of 18 years, a disease duration of less than one year, and a diagnosis of RA assessed by a rheumatologist according to the 1987 American College of Rheuamtology (ACR) criteria (Arnett et al., 1988). Patients were informed by their rheumatologists about this study during the first routine visit in which ACR criteria were assessed. One hundred patients agreed to participate and received a questionnaire during the second routine visit which was scheduled about three weeks later (range 0-12 weeks). This second visit was also the starting point for the second-line anti-rheumatic medication. Correctly completed questionnaires were returned by 95 patients. One year later, 91 patients completed the questionnaires again. In none of the patients remission occurred. The sample was predominantly female (70%), married or living together with a partner (74%), with primary (34%) or secondary (53%) education. The mean age was 57 years (range 20-82 years). The medication of the patients was as follows: 31% patients were on non-steroidal anti-inflammatory drugs (NSAID) alone; the other were on NSAID in combination with methotrexate (25%), intramuscular gold (16%), hydroxychloroquine (14%), or prednisone (14%). Means of psychological distress and clinical status measures of the patients on first and second assessments are presented in Table 1.

Measures

Psychological distress in the past month was measured with the Anxiety and Depressed Mood scales of the Impact of Rheumatic diseases on General health and Lifestyle (IRGL; Huiskes et al., 1990a). The IRGL is partly derived from the Arthritis Impact Measurement Scales (AIMS; Meenan et al., 1980) and measures the physical, psychological, and social aspects of health status in patients with rheumatic diseases. The Anxiety scale (10 items) of the IRGL is a condensed version of the the Dutch State Anxiety Scale (STAI-DY; Spielberger et al., 1970; van der Ploeg et al., 1980). The Depressive Mood scale (6 items) of the IRGL is derived from a questionnaire of Zwart and Spooren (1982). Any of these scales contains somatic items which could reflect the RA disease process or consequences. Items of the IRGL scales are scored on a 4 or 5-point Likert-scale. In previous research, reliability and validity of the IRGL scales were shown to be highly satisfactory (Huiskes et al., 1990a).

Clinical status measures were obtained through standardized clinical and laboratory data as well as self-report measures. Clinical and laboratory data were collected on erythrocyte sedimentation rate (ESR), joint scores according to the

method described by Thompson (1987), and grip strength measured by a Martin vigorimeter (mean of three measurements of each hand was calculated). Self-report measures included assessments of pain and functional status. Pain in the past month were assessed by the Pain scale (6 items) of the IRGL. Self-reports of functional status in the past month were assessed by the Mobility (7 items) and Self-care scale (8 items) of the IRGL.

Disease impact on daily life was measured by the Disease Impact scale of the IRGL (10 items) referring to the general impact the disease has on several domains of daily life (i.e., work, leisure, relationships, sexuality, food).

Stressful life events were measured with a Dutch version of the Life Experience Survey (LES), assessing the occurrence of 60 events concerning health, work and financial situation, relationships, living, and personal matters during the past 12 months (Sarason et al., 1978; van de Willige et al., 1985). In order to minimize confounding effects with disease impact, four disease related events were excluded (admission to hospital, surgical operation, occurrence of severe disease, important change in health status).

Social support in the past six months was measured by the social functioning scales of the IRGL, reflecting a quantitative and qualitative aspect of social support: the size of the social network was measured through the index Number of Friends; perceived availability of support was assessed by the scale Perceived Support (5 items).

Coping strategies were assessed using the Utrecht Coping List (UCL; Schreurs et al., 1993), partly adopted from Westbrook (1979). Patients were instructed to indicate the extent to which they used different kinds of coping behavior in dealing with stressors of everyday life. Items were scored on a 4-point Likert scale. Four of the seven scales of the questionnaire were used in the present study: Tackling Problems Actively (7 items), Comforting Cognitions (5 items), Distraction (8 items) and Avoidance (8 items). Reliability and validity have been shown to be satisfactory (Sanderman & Ormel, 1992).

Statistical Analyses

Because of skewed distributions of scores at depressed mood and life events, square root transformations were applied. Social network scores were categorized according to norm classes (Huiskes et al., 1990a). In order to examine the relative contribution of demographic variables, clinical status, disease impact on daily life, life events, social support, and coping strategies on psychological distress shortly after diagnosis, hierarchical multiple regression analysis was performed with all predictors which were significantly related to at least one of the measures of psychological distress (anxiety or depressed mood). In order to predict the course of psychological distress within one year, the same procedure was followed for the longitudinal data with distress levels about one year after diagnosis, entering distress levels shortly after diagnosis at the first step. Bivariate associations

between all variables were calculated with Pearson correlation coefficients. Differences between means of the first and second assessment were tested with Student's *t*-test and Wilcoxon Signed Rank Test in the case of ESR and Thompson's joint score. All statistical analyses were carried out with the SPSS 6.1/Windows statistical package with a minimum of 88 patients sharing complete datasets.

RESULTS

Level of Psychological Distress

Patients exhibited relatively high levels of psychological distress. In comparison to norm groups of the general population obtained by van der Ploeg et al. (1980) and Zwart and Spooren (1982), this group of recently diagnosed RA patients reported significantly higher levels of depressed mood ($t = 4.42$, $p < 0.01$) and anxiety ($t = 4.92$, $p < 0.01$). When examining risk groups, 27 and 38 patients (28% and 40%), respectively, had an equal or higher anxiety and depressed mood value than the mean score of DSM-III diagnosed psychiatric outpatients, while 17 and 19 patients (18% and 20%), respectively, reported an equal or higher level than the mean score of patients with a clinical anxiety or depression diagnosis (van der Ploeg et al., 1980; Zwart & Spooren, 1982).

Table 1 Means and SDs of Psychological Distress and Clinical Status Shortly After the Diagnosis (T1) and 1 Year Later (T2)

	T1		T2	
Variable (range)	M	SD	M	SD
Psychological distress				
Anxiety (10-40)	19.2	6.7	19.0	6.8
Depressed mood [a](0-5)	1.5	1.3	1.3	1.3
Clinical status				
ESR (1-140 mm 1st hr)	30.9	23.3	23.7	22.4
Joint score (0-534)	96.9	95.9	66.0	77.4
Grip strength (0-130 kPa)	32.7	23.0	40.4	26.2
Pain (6-25)	15.6	4.9	14.1	5.3
Mobility (7-28)	19.6	6.1	20.9	5.7
Self-care (8-32)	24.3	5.9	25.3	5.6

[a] Square root.

Predictors of Psychological Distress Shortly After Diagnosis and 1 Year Later

Hierarchical multiple regression analyses were used to examine the relationship between demographic variables (sex, age, educational level), clinical status (ESR, joint score, grip strength, mobility, self-care, pain), disease impact on daily life, life events, social support and coping strategies, and the level of psychological distress shortly after diagnosis. Only those variables were entered in the regression model which were significantly related to at least one of the measures of psychological distress (anxiety or depressed mood at T1); i.e. sex, pain, and self-report measures of functional status (mobility and self-care), disease impact on daily life, life events, social support and coping strategies (distraction and avoidance) (see Table 2). The results of the last step of the cross-sectional regression analysis are shown in the left columns of Table 2.

At step 1, sex (being female) contributed 5% to the variance in anxiety (Fchange = 5.96, $p < 0.05$), but it did not explain any significant variance in depressed mood. Clinical status variables (pain, mobility, self-care) entered at step 2 added 12% of the variance in anxiety (Fchange = 5.46, $p < 0.01$) and 20% in depressed mood (Fchange = 8.51, $p < 0.001$). In order to analyse the relative contribution of pain and functional status (mobility and self-care), both were also separately entered into the model. Pain accounted for significant variance when entered either before or after functional status. Functional status failed to make a significant contribution if it was entered after pain, suggesting that pain mediated the relationship between functional status and distress. At step 3, disease impact on daily life contributed a further 11% to the variance in anxiety (Fchange = 14.37, $p < 0.001$) and 7% of the variance in depressed mood (Fchange = 9.64, $p < 0.01$). Life events entered at step 4 explained an additional 9% of the variance in anxiety (Fchange = 12.32; $p < 0.001$), but did not contribute to the variance in depressed mood. When life events were entered before disease impact, the same results were revealed as in the reversed order. Social support at step 5 added 5% to the variance in anxiety (Fchange = 5.14, $p < 0.01$), and 4% to the variance in depressed mood (Fchange = 3.08, $p = 0.05$). If social network and perceived support were entered separately, only perceived support made a significant contribution to the variance in anxiety and depressed mood. Coping strategies at step 6 did not add any more significant variance to anxiety or depressed mood. Also when entry order of social support and coping strategies was reversed, the latter did not make a significant contribution. All independent variables accounted for a total amount of 44% of the variance in anxiety and 36% of the variance in depressed mood.

One year after diagnosis, psychological distress was related to the same set of predictors at that time. Entering these predictors in multiple regression analyses, they explained even 55% variance in anxiety and 45% in depressed mood. The greater amount of explained variance mainly arose from a stronger contribution of social support variables (9% in anxiety and 8% in depressed mood), and a

significant contribution of the coping strategies (avoidance and distraction) in anxiety and depressed mood (4% and 6%, respectively).

Taken together, the amount of psychological distress shortly after diagnosis could be best predicted by female sex, high levels of pain and disease impact on daily life, the occurence of more life events and low levels of perceived social support. Pain seems to mediate the relationship between functional status and psychological distress. One year after diagnosis, relationships were replicated, but the contribution of social and personal coping resources were stronger.

Predictors of the Course of Psychological Distress in the First Year After Diagnosis

Change in clinical status and psychological distress 1 year after diagnosis. One year after diagnosis, there was a mean decrease in five of the six clinical status measures (see Table 1). Improvements in clinical status were reflected by a decrease in ESR (z = -3.64, $p < 0.001$), Thompson's joint scores (z = -3.24, $p < 0.001$), and pain (t = 2.71, $p < 0.01$) as well as an increase in grip strength (t = -4.27, $p < 0.001$) and mobility (t = -3.05, $p < 0.01$) one year after diagnosis. However, psychological distress was rather stable (Table 1). The mean levels of anxiety and depressed mood were not changed after one year. Looking at individual changes, improvements (more than 0.5 SD) occurred in 18 patients (19%) in anxiety and 17 patients (18%) in depressed mood. A deterioriation in psychological distress occurred in 13 patients (15%) in anxiety and 24 patients (25%) in depressed mood.

Predictors of change in psychological distress. In order to evaluate the extent to which the independent variables shortly after diagnosis predicted the individual patient's course of psychological distress within one year, a hierarchical multiple regression analysis was conducted with the distress levels one year after diagnosis, entering distress levels shortly after diagnosis at the first step. Again, only those variables were entered in the regression model which were significantly related to at least one of the outcome measures. For this purpose, residual gain scores of anxiety of depressed mood were calculated. Of the set of predictors, only sex, ESR and social network were significantly related to change in anxiety or depressed mood (see Table 2). Hierarchical regression analyses indicated a strong autoregressive effect for psychological distress over time, accounting for 57% of the variance in anxiety (Fchange = 118.23, $p < 0.001$) and for 43% in depressed mood (Fchange = 68.95, $p < 0.001$). At step 2 and 3, sex (being female) contributed 2% and high levels of ESR contributed 1% to the variance in anxiety change (Fchange = 5.17, $p < 0.05$; Fchange = 3.84, $p < 0.05$ respectively), but did not add variance to depressed mood change. At step 4, the size of the social network did not make a significant contribution in anxiety change, but a smaller social network added 3% to the variance in depressed mood change (Fchange = 4.83, $p < 0.05$).

Table 2 Stepwise Multiple Regression Predicting Psychological Distress at Study Entry (T1) and 1 Year Later (T2) from Selected Predictors at Study Entry [a]

	Anxiety T1			Depressed mood T1			Anxiety T2			Depressed Mood T2		
	r	β	Δ R^2	r	β	Δ R^2	r	β	Δ R^2	r	β	Δ R^2
Psychological distress T1												
Anxiety [b]							.76**	.68**	.57**			
Depressed mood [b]										.66**	.61**	.43**
Demographic variables			.05*			.02			.02*			.00
Age	-.17			-.11			.07			.16		
Sex	.24*	.11		.17	.09		.21*	.13		.13	.06	
Education	.07			.02			-.04			-.02		
Clinical status T1			.12**			.20**			.01*			.00
ESR	.08			.05			.21*	.14*		.10	.08	
Thompson score	.13			.12			-.03			.05		
Grip strength	-.15			-.05			-.14			-.12		
Pain	.29**	.03		.40**	.20*		.00			-.11		
Mobility	-.29**	.04		-.34**	-.13		-.17			-.14		
Self-care	-.31**	-.05		-.21*	.11		-.15			-.16		
Disease impact T1	.54**	.37**	.11**	.52**	.31**	.07**	.04			-.06		
Life events T1	.40**	.24**	.09**	.25*	.02	.00	-.14			-.02		
Social Support T1			.05**			.04*			.01			.03*
Social network	-.28**	-.11		-.21*	-.09		-.20	-.11		-.22*	-.18*	
Perceived support	-.39**	-.20*		-.30**	-.18*		.15			-.09		
Coping strategies T1			.02			.03						
Tackl. problems actively	-.15			-.17			-.05			-.03		
Comforting cognitions	-.07			-.10			-.19			-.04		
Distraction	.22*	.03		.29**	.19*		-.13			-.04		
Avoidance	.31**	.16		.30**	.07		.11			.13		
Total adj. Δ R^2			.44**			.36**			.61**			.46**

[a] Two-tailed probabilities of Δ R^2 (*F*-change), *r* (calculated with anxiety and depressed mood T1 and the residual gain scores), and β (*t*-test). Selection criterion was the significant association with one of the measures of psychological distress (anxiety or depressed mood T1 and the residual gain scores).

[b] Zero order correlation. * $p < 0.05$ ** $p < 0.01$.

Due to the significant mean improvements in clinical status, the extent to which changes in psychological distress were related to parallel changes in clinical status were also examined. Pearson correlation coefficients revealed that a decrease in anxiety and depressed mood was significantly related to a decrease in pain (r = 0.42, $p < 0.001$; r = 0.23, $p < 0.05$, respectively) and an increase in mobility (r = -0.35, $p < 0.01$; r = -0.36, $p < 0.01$, respectively) and self-care (r = -0.32, $p < 0.01$; r = -0.21, $p < 0.05$, respectively), but not to changes in ESR, Thompson score or grip strength. If change in pain, mobility, and self-care were entered into the regression analysis at step 4 (after sex, ESR, and social network), they were responsible for a further 8% of the variance in anxiety and 5% variance in depressed mood (Fchange = 7.99, $p < 0.001$; Fchange = 3.48, $p < 0.05$, respectively), accounting for a total variance of 69% in anxiety and 51% in depressed mood.

Taken together, a decrease in anxiety in the first year after the diagnosis was related to male sex and initial lower levels of ESR. A decrease in depressed mood was associated with an initially larger social network. In addition, a decrease in both distress measures were related to simultaneous improvements in clinical status.

DISCUSSION

The amount and prevalence of psychological distress is relatively high in recently diagnosed RA patients. Our sample reported significantly higher distress levels than healthy subjects with a depression and anxiety prevalence of about 20%, which has also been reported in patients with established disease (Bishop et al., 1987; Frank et al., 1988; Murphy et al., 1988). In line with research of Meenan et al. (1991), it can be concluded that recently diagnosed patients do not differ dramatically from chronic patients in the amount of distress they are experiencing. Psychological distress also appeared to be a rather stable phenomenon for our group RA patients, and an adaptation to the disease seems not to have taken place (yet) in the first year after diagnosis. Psychological adaptation may be indicated by a reduction or stability of distress with a simultaneous deterioriation of the disease state. While clinical status improved, probably due the positive effects of the medication therapy (van der Heide et al., 1994b), the mean level of psychological distress did not change, and percentages of patients whose distress improved or deterioriated were about the same.

For the understanding of psychological distress shortly after diagnosis, the multimodal assessment of demographic variables, clinical and life stressors, and social resources was shown to be important in the current study. The amount of distress shortly after diagnosis could be substantially explained by sex, functional

status and pain, disease impact at daily life, stressful life events, and perceived social support. All these factors were also related to the amount of distress one year later. Their relationship with distress therefore seems to be relative stable within the first year of the disease.

How do our findings relate to findings in studies of patients with RA of longer disease duration? The role of pain and functional status with regard to distress have been previously demonstrated in recently diagnosed patients (van der Heide et al., 1994a) and in patients with more established disease (Newman et al., 1989; Brown, 1990; Nicassio & Wallston, 1992; Wolfe & Hawley, 1993). In our sample of recently diagnosed patients, pain mediates the relationship between functional status and distress; a finding that was not observed in patients with longstanding RA (Wolfe & Hawley, 1993). A worse functional status, such as found in longstanding RA (Wolfe & Cathey, 1991), may figure as an additional stressor to pain, while the less worse functional status of recently diagnosed patients may be more clearly associated with pain. Moreover, pain and functional status may be more clearly related to current disease activity in the early phases of RA, while being distinct outcomes of past disease activity in the advanced phases. In addition to pain and functional status, the experienced impact the disease has on daily life, such as work, recreation and relationships was very important for higher levels of distress, as has also been suggested in studies of patients with longstanding RA (Devins et al., 1992; Brons et al., 1993; Katz & Yelin, 1995). Less evidence in patients with longstanding RA has been found for the experience of major life events (e.g., Brons et al., 1993) which figures as an additional stressor in anxiety in recently diagnosed patients. Results suggest that the additional effects of clinical and life stressors are especially important at an early stage of the disease when patients are less experienced with the stressors of a chronic disease. Irrespective of stressors, qualitative aspects of social support, such as the perceived availability of support, seem to be beneficial for the amount of distress in recently diagnosed patients, as has been demonstrated in patients with a more established disease (i.e., Brown et al., 1989b; Goodenow et al., 1990). Considering the greater amount of variance social support explained one year later, this effect might increase with longer disease duration. Although the suggested direction of the predictors has been partly confirmed in patients with established disease, the direction of the relationships may be reversed or at least be reciprocal. For instance, it may be the case that higher distress levels also cause a higher sensitivity to pain, lead to the report of the occurence of more life events and affect the perception of experienced disease impact on daily life and receipt of support.

Predictors for an increase in psychological distress in the first year after diagnosis were female sex, an initially higher inflammatory activity as indicated by ESR, and an initially smaller social network. Women did not only have higher levels of anxiety shortly after diagnosis, but their sex in itself was also a risk factor for an increase in anxiety after one year. After taking the influence of sex into

account, patients with a greater inflammatory activity, indicated by higher levels of ESR shortly after diagnosis, had a higher risk of an increase in anxiety one year later. However, ESR was not related to the amount of anxiety shortly after diagnosis. While the amount of psychological distress shortly after diagnosis is related to directly experienced health outcome measures such as pain and functional status, measures more clearly reflecting the disease process such as ESR are predictive of the course of distress in the first year of the disease. Longitudinal studies in patients with longstanding RA have demonstrated that sex as well as ESR are both predictors of future functional status (Sherrer et al., 1987). Considering that the course of psychological distress was relative strongly related to the course of functional status and pain in the first year after diagnosis in our sample, the relation between the predictors and the course of distress may be parallel to the development of function. Posthoc analyses indeed demonstrated that female sex and higher levels of ESR both also predicted a worse functional status after one year (self-care and grip strength, respectively). Results suggest that the course of psychological distress in the first year of the disease depend on similar factors than the course of the clinical outcome. Indicators of psychological adaptation may be therefore only visible in patients with a less severe disease process and less ongoing disability.

For changes in depressed mood, the magnitude of the social network predicted changes after one year. Patients who were less imbedded in a social network shortly after diagnosis showed an increase in depressed mood after one year. Such a prognostic effect for the quantitative aspect of social support seems to be in contrast with findings in patients with a more established disease (e.g., Brown et al., 1989b). An extended social network which probably offers broad resources of support (emotional as well as instrumental) seems to be more important for the psychological adaptation of a patient shortly after diagnosis, when usual patterns of life are disturbed and many life domains have to be reorganized, than at a more progressive stage of the disease. Network-enhancing interventions, for example, by offering support groups and facilities of interdisciplinary health care teams, may promote the well-being of recently diagnosed patients.

Our predictors allow the identification of risk factors for an increase in psychological distress in the first year after diagnosis, but their overall explained variance was rather small. One explanation may be that one year is too short to discover a larger influence of psychological factors on the development of distress. Probably due to beneficial effects of the medication therapy, psychological changes instead covary more strongly with changes in clinical status. Studies in patients with a longer disease duration partly failed to find a relationship between changes in clinical status and psychological functioning (McFarlane & Brooks, 1988). If associations were found, they only occurred in patients with relatively dramatic flares of disease activity (Bishop et al., 1987) or seem to be most strong over a short period of time (Wolfe & Hawley, 1993). At a later phase of the

disease, the function of social and personal coping resources seems to increase. In our study, contribution of social support was stronger one year after diagnosis than on first assessment, and coping strategies did modify the relationship between stressors and distress only one year after diagnosis. After a personally threatening event, such as the occurrence of a chronic disease, the general way to cope with stress of daily life may be disturbed, old types of coping behavior may not be appropriate any more to deal with new stressors, and new behavior has not been established yet. Effects of readjustment processes, which derive from the personal coping resources available, may be part of a more longstanding process and be only visible over a longer period of time and at later stages of the disease.

Results of our study underline the importance of a multimodal assessment and consultation in recently diagnosed patients, including demographic variables, clinical and life stressors, and social support characteristics which are relevant for the understanding of distress shortly after diagnosis and which highlight risk factors for less psychological adjustment to the disease in the first year. Besides medical treatment, psychological adjustment of patients may be optimized by support-enhancing health care facilities in the first year after diagnosis. The influence of personal coping factors seems to be more important at a later stage of the disease.

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3

3.1 Coping and Social Support

3.1.3 Predictors of psychological distress

3.1.3.2 Long-term predictors of anxiety and depressed mood in early rheumatoid arthritis: A 3 and 5-year follow-up

Evers, A.W.M., Kraaimaat, F.W., Geenen, R., Jacobs, J.W.G. & Bijlsma, J.W.J. (2002). Long-term predictors of anxiety and depressed mood in early rheumatoid arthritis: A 3 and 5-year follow-up. *Journal of Rheumatology, 29*, 2327-2336.

ABSTRACT

Heightened levels of anxiety and depressed mood are known to be common consequences of rheumatoid arthritis (RA). We examined the role of stress-vulnerability factors in the long-term course of anxiety and depressed mood in patients with early rheumatoid arthritis. Specifically, the role of personality characteristics (neuroticism, extraversion), physical and psychological stressors (clinical status, disease impact on daily life, major life events), and coping and social support at the time of diagnosis were studied to predict changes in anxiety and depressed mood 3 and 5 years later. For this purpose, anxiety and depressed mood, predicted from clinical and self-reported assessments of stress-vulnerability factors at the time of diagnosis in 78 patients with RA, were assessed again after 3 and 5 years. Results indicated that a worse clinical status, more neuroticism, and lower education level at the time of diagnosis were all significantly related to increased psychological distress at the 3 and 5-year follow-ups. However, the personality characteristics of neuroticism proved to be the most consistent and effective predictor of anxiety and depressed mood after 3 and 5 years, irrespective of initial distress levels, biomedical factors, use of medication, and other stressors or vulnerability factors. Results of this study demonstrate the prognostic value of personality characteristics for long-term susceptibility to distress in patients with early RA, and emphasize the importance of paying close attention to factors unrelated to RA when screening for patients at risk.

INTRODUCTION

The diagnosis of a chronic, disabling disease such as rheumatoid arthritis (RA) can have a significant impact on an individual's daily life, since patients have to deal with a potentially uncontrollable, unpredictable, long-term condition that may affect almost all aspects of their physical, psychological, and social functioning (Fex et al., 1998; van Jaarsveld et al., 1998). Although most patients seem to adjust well to the changes imposed by the disease and find an acceptable level of well-being, about 20% suffer heightened levels of anxiety and depression, comparable to those of people with anxiety and depressive disorders (Frank et al., 1988; Murphy et al., 1988; Hawley & Wolfe, 1993; Smedstad et al., 1996; Evers et al., 1997). To understand the individual variability in psychological adjustment to RA, research has focused on identifying risk factors for patients for whom the confrontation with the chronic disease seem to exceed their adaptive capacities and who become highly distressed.

On the basis of stress-vulnerability models (Brown & Harris, 1978; Lazarus & Folkman, 1984; Leventhal et al., 1984; Steptoe, 1998), different stressors and vulnerability factors have been proposed to affect distress levels in patients with RA. For example, chronic, disease-related stressors, such as a worse clinical status due to more disease activity, pain and functional disability, and the psychological impact of the disease on daily life due to limited possibilities in daily activities or changes in social relationships have been shown to affect anxiety and depression in patients with RA (Hawley & Wolfe, 1988; Brown, 1990; van Lankveld et al., 1993; van der Heide et al., 1994a). Further, major stressful life events are known to be important predictors of long-term distress in the general population (Kessler, 1997; Mazure, 1998) and may similarly affect distress in patients with RA (Grady et al., 1991; Affleck et al., 1994; Dekkers et al., 2001). Regarding vulnerability factors, the manner of coping with stress and the level of social support have been shown to have an effect on well-being in patients with RA and direct, mediating, or moderating effects on the stress-illness relationship. Based on general distinctions between active, problem-focused coping and passive, avoidant coping, it has repeatedly been found that the use of more passive coping strategies is prospectively related to heightened distress in RA (Felton & Revenson, 1984; Brown et al., 1989a; Smith & Wallston, 1992; Scharloo et al., 1999). Similarly, patients with RA with less social support - in terms of the quantity, i.e., the size of their social network, as well as the quality, i.e., the perceived availability of support - have been shown to adjust less successfully to their chronic condition (Brown et al., 1989b; Affleck et al., 1994; Evers et al., 1997). Attention has also been directed to the influence of relatively stable personality characteristics as vulnerability factors for maladjustment in patients with RA (Affleck et al., 1992; Persson et al., 1999). Two dimensions in particular, neuroticism, the tendency to be relatively more tense and emotionally unstable, and extraversion, the tendency to

be relatively more sociable and impulsive, are related to health and well-being in various chronic diseases, including RA (Harkins et al, 1989; Affleck et al., 1992; Smith et al., 1995; Persson et al., 1999; Phillips & Gatchel, 2000). In addition, personality characteristics are assumed to be crucial in accounting for the effects of stressors, coping, and social support on long-term distress, since people with high neuroticism and low extraversion report more physical complaints and stressful life events, experience less social support, and engage in more dysfunctional coping behavior (Costa & McCrae, 1987; Harkins et al, 1989; Watson & Pennebaker, 1989; McCrae, 1990; Affleck et al., 1992; Smith et al., 1995; Persson et al., 1999; Phillips & Gatchel, 2000).

So far, empirical evidence supports a link between stress-vulnerability factors and psychological distress in RA patients. However, definite conclusions about the specific kinds of variables and their relative contributions cannot be drawn from present research, since a comprehensive test of various stressors and vulnerability factors has rarely been conducted. In addition, patients have usually been followed for relatively short periods of time in prospective studies, and the extent to which the kinds of predictors and strength and direction of effects for short-term outcomes can be generalized to long-term outcomes is largely unknown (Suls & Fletcher, 1985). Moreover, stressors and vulnerability factors have usually been assessed in patients with longstanding RA. Stress-vulnerability factors are known to be affected by the disease process, its biopsychosocial consequences, and pharmacological treatment (van Lankveld et al., 1993; Fex et al., 1998; van Jaarsveld et al., 1998, 2000; Penninx et al., 1999), and they may consequently be more validly assessed in recently diagnosed patients. In addition, an identification of stress-vulnerability factors in recently diagnosed patients may allow patients to be screened at the earliest possible time after contacting a rheumatologist, at diagnosis.

We investigated the predictive value of a comprehensive set of stress-vulnerability factors at the time of diagnosis for the long-term course of psychological distress in early RA. The role of stress-vulnerability factors at the time of diagnosis has previously been studied by our group, to predict psychological distress in the first year after diagnosis (Evers et al., 1997). However, stressors and vulnerability factors scarcely predicted the course of distress in the first year after diagnosis. In this study, follow-up results after 3 and 5 years are presented. Specifically, the role of personality characteristics (neuroticism, extraversion), stressors (clinical status, disease impact on daily life, major life events), coping, and social support at the time of diagnosis was studied to predict anxiety and depressed mood 3 and 5 years later. It was expected that more neuroticism and less extraversion, higher levels of stressors, greater use of passive coping, and less use of active coping as well as less social support would predict an increase in psychological distress after 3 and 5 years. We further examined whether stressors, coping, and social support account for the effects of

personality characteristics on long-term psychological distress (mediating effects of stressors, coping, and social support). Finally, we explored whether the maladaptive effects of stressors on psychological distress might be increased in patients with more unfavorable vulnerability factors (moderating effects of personality characteristics, coping, and social support on stressors).

METHODS

Sample and Procedure

The study sample consisted of outpatients with recently diagnosed RA from five hospitals in the Utrecht area of the Netherlands. All patients participated in one of two medical trials of second-line anti-rheumatic drugs (van Jaarsveld et al., 2000; van Everdingen et al., 2002). Inclusion criteria for the medical trials were a minimum age of 18 years, diagnosis according to the 1987 American College of Rheumatology (ACR) criteria (Arnett et al., 1988), and a duration of disease of less than one year. Exclusion criteria were comorbid conditions that might interfere with one of the medication strategies (such as malignancy, cardiac, respiratory, hepatic, and renal insufficiency), previous or current treatment with second-line anti-rheumatic drugs, use of glucocorticoids, cytotoxic or immunosuppressive drugs, possible pregnancy or breast feeding, and psychiatric or mental disturbances that severely interfere with adherence to the study protocol. All incoming patients from the hospitals who met the inclusion criteria were asked to participate in the medical trials. About 25% of the patients did not agree to be randomized, but there were no differences found between these patients and participants in terms of their levels of disease activity. From the remaining 394 patients participating in the medical trials, a subgroup of 100 patients were randomly selected for participation in the present study.

Patients were informed about this study by their rheumatologists during their first visit, when ACR criteria were assessed. About three weeks later (range 0-12 weeks), clinical and self-report data were assessed during their second visit. This second visit was also the starting point for the prospective medical trials. Five patients did not return the questionnaires at this assessment point, resulting in 95 patients who participated in the study at the time of diagnosis. In addition to assessing clinical and self-report data at the beginning of the study and at the 1-year follow-up (Evers et al., 1997), data on disease activity, functional disability, pain, and psychological distress was again collected at the 3 and 5-year follow-ups.

Of the 95 patients who correctlly completed self-report data at the first assessment, 78 (82%) completed all assessment points during the 5-year study period. Participants in the follow-up were predominantly female (69%), married or living with a partner (76%), and had a primary (32%) or secondary (57%)

education level. Mean age at the time of entering the study was 57 years (range 20-82 years). In terms of dropouts, 7 patients died, 2 moved, 1 was in remission and not longer treated in the rheumatology outpatient clinic, and 7 did not complete the questionnaires for the follow-up assessments. When entering the study, dropouts did not significantly differ from participants in terms of demographic variables (sex, age, marital status, education level), disease activity, pain, functional disability, disease impact on daily life, experience of major life events, personality dimensions of extraversion, coping, or social support. However, dropouts scored higher on both indicators of psychological distress (t = 2.61, $p < 0.05$ for anxiety and $t = 2.24$, $p < 0.05$ for depressed mood) and on the personality dimension of neuroticism ($t = 2.87$, $p < 0.01$) than patients who completed all assessment points.

When included in the medication trials, all patients were randomly assigned to one of the medication strategies. The drug trials lasted at least two years for all patients, but medication strategies were continued unless adverse reactions of ineffectiveness made discontinuation inevitable in the opinion of the attending doctor. In that case, one of the other medication strategies from the trials was usually prescribed. The distribution of medication strategies was as follows: 30% and 23% of the patients used non-steroidal anti-inflammatory drugs (NSAID) alone at first assessment and at the 5-year follow-up, respectively; the other patients took NSAID in combination with methotrexate (30% and 49%, respectively), intramuscular gold (14% at both assessment points), hydroxychloroquine (15% and 9%), prednisone (11% and 1%) or other second-line medication, prescribed only for individual patients (4% at the 5-year follow-up). At the 5-year follow-up, 31% of the patients still used the initially prescribed medication (6% NSAID alone, 17% methotrexate, 4% intramuscular gold, 3% hydroxychloroquine, and 1% prednisone), while 65% used another medication strategy from the drug trial (17% NSAID alone, 32% methotrexate, 10% intramuscular gold, 6% hydroxy-chloroquine), and 4% of the patients used another second-line medication than those used in the medication trials. Finally, no patient in the psychosocial study met removal criteria during the study period, i.e. the occurrence of other serious disease processes or an incorrect RA diagnosis.

Measures

Demographic variables were assessed with a general checklist for patients' sex (0 = male, 1 = female), age, and marital status (0 = unmarried, 1 = married). In addition, education level was measured using 7 categories that can be classified as primary, secondary, and tertiary education levels, representing on average 7, 12, and 17 years of education, respectively.

Disease activity was determined by erythrocyte sedimentation rate (ESR; 1-140 mm/h) and by Thompson's joint score ratings of the simultaneous presence of swelling and pain in 38 joints (Thompson, 1987). A composite score of both

variables was used, in accord with regular use of composite scores of disease activity that consist of at least ESR or another acute phase reactant and a joint score (e.g. the modified Disease Activity Score, Prevoo et al., 1995). The composite score was calculated by adding the standardized scores (*z*-scores) of both indicators.

Functional disability was assessed using a composite score of one clinical measure and two self-report measures (Evers et al., 1998a). The clinical measure consisted of grip strength assessments with a Martin vigorimeter (the mean of three measurements on both hands was calculated). Self-reported functional disability was assessed with the Mobility and Self-care scales of the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL; Huiskes et al., 1990a; Evers et al., 1998b), a questionnaire derived from the Arithritis Impact Measurement Scales (AIMS, Meenan et al., 1980), which assesses physical, psychological, and social health in patients with rheumatic diseases. Research has shown that the reliability and validity of the IRGL scales are highly satisfactory (Huiskes et al., 1990a; Evers et al., 1998b). The Mobility and Self-care scales, which assess the functional capacities of the lower and upper extremities, respectively, over the last month (15 items) have been shown to be highly comparable to the AIMS physical functioning scales (Evers et al., 1998b). Cronbach's alpha in the present study was 0.89 for both scales. A composite score of the clinical measure of grip strength and the two Mobility and Self-care self-report scales was calculated by adding the standardized scores (*z*-scores) of all indicators. A higher composite score indicates higher levels of functional disability.

Pain was assessed with the IRGL Pain scale (6 items), measuring the severity and frequency of painful episodes and swollen joints and duration of early morning stiffness in the last month. Cronbach's alpha in the present study was 0.88.

Psychological distress was measured with the IRGL Anxiety and Depressed Mood scales. The Anxiety scale is a shortened version of the Dutch State Anxiety Scale (10 items) (Spielberger et al., 1970; van der Ploeg et al., 1980), assessing anxiety levels in the last month. The Depressed Mood scale (6 items) is derived from Zwart and Spooren's questionnaire (Zwart & Spooren, 1982) and assesses various depressed mood states over the previous week. Cronbach's alpha for the Anxiety and Depressed Mood scales in the present study were 0.91 and 0.94, respectively.

Disease impact on daily life was measured with the IRGL Disease Impact scale (10 items), which assesses the general impact of the disease on several areas of daily life (i.e. work, leisure, relationships, sexuality, eating). Cronbach's alpha in the present study was 0.87.

Major life events were measured with a Dutch version of the Life Experience Survey (LES), assessing the occurrence of 60 stressful events related to health, work, financial circumstances, relationships, living, and personal matters in the last 12 months (Sarason et al., 1978; van de Willige et al., 1985). To minimize

confounding effects between major life events and disease impact on daily life, four disease-related events were excluded (occurrence of severe disease, important changes in health status, hospital admission, surgery).

Personality dimensions, i.e., neuroticism and extraversion, were measured with a Dutch version of the Eysenck Personality Questionnaire (EPQ; Wilde, 1970; Eysenck & Eysenck, 1991). Cronbach's alpha in this study was 0.90 for neuroticism and 0.79 for extraversion.

Coping strategies were assessed with the Utrecht Coping List (UCL; Schreurs et al., 1993), a well-documented coping questionnaire used in the Netherlands (e.g., Evers et al., 1997; Scharloo et al., 1999), adopted from Westbrook (Westbrook, 1979), which measures on a 4-point Likert scale active and passive coping strategies when dealing with everyday problems. Active coping was assessed with the Problem Focusing scale (7 items), measuring cognitive and behavioral efforts to apply goal-oriented problem-solving strategies. Passive coping was measured with the Avoidance scale (8 items), measuring cognitive and behavioral attempts to avoid, escape from, and acquiesce when facing everyday problems. Cronbach's alpha in the study was 0.85 for the Active and 0.67 for the Passive coping scales.

Social support in the past six months was measured with the IRGL social functioning scales, reflecting a quantitative and qualitative aspect of social support. The quantitative aspect was assessed by the size of the social network, i.e. the number of friends and family members with whom patients associate. The qualitative aspect was measured with the Perceived Support scale (5 items), inquiring about perceived availability of emotional and instrumental support. Cronbach's alpha for the Perceived Support scale was 0.88.

Statistical Analyses

The number of patients scoring on anxiety and depressed mood equal to or higher than mean scores of psychiatric outpatients and patients with a clinical anxiety and depression diagnosis was determined by comparing scores to mean scores of representative norm groups in Dutch populations of psychiatric outpatients and patients with a clinical anxiety or depression diagnosis (van der Ploeg et al., 1980; Zwart & Spooren, 1982). To study mean linear changes in clinical status and psychological distress over time, a general linear model with repeated measurements was applied for every indicator of clinical status (disease activity, functional disability, pain) and psychological distress (anxiety and depressed mood), using the variables at the different assessment points as dependent variables, followed by posthoc tests in the case of significant linear changes.

To explore the relationship between stress-vulnerability factors at the time of diagnosis and changes in anxiety and depressed mood after three and five years, Pearson correlation coefficients were calculated between the stress-vulnerability

factors at first assessment and the change scores of anxiety and depressed mood at the 3 and 5-year follow-up. Residual gain scores were used to measure changes in anxiety and depressed mood (Kerlinger, 1975). Residual gain scores take into account the individual baseline levels and control for regression to the mean effects. Residual gain scores were calculated by regressing the outcome variable at the follow-up assessment (e.g. depressed mood at the 3-year follow-up) on the baseline score of the outcome measure (e.g. depressed mood at the time of diagnosis). Sequential regression analyses were then performed to study the relative contribution of the stress-vulnerability factors to anxiety and depressed mood at the 3 and 5-year follow-up. Anxiety and depressed mood at the 3 and 5-year follow-up were used as dependent variables. In the first step, anxiety and depressed mood assessed at the time of diagnosis were entered, reflecting residual gain scores. In the following steps, the different predictors were entered that were significantly related to the residual gain scores of anxiety and depressed mood at at least one follow-up assessment. These predictors were entered in consecutive steps in the regression analyses to test their additional contribution in terms of significant *F*change, after taking into account the variance explained by the other predictors. The grouping of variables in a step as well as the entry order of the steps was determined a priori by the stress-vulnerability model (e.g., indicators of clinical status were entered in one step together, and they were entered after the more stable characteristics of demographic variables and personality characteristics). However, entry order between steps was also changed to study the single contribution of every step, above the variance already explained by the baseline scores of anxiety and depressed mood. The strength of the beta (standardized regression coefficients) and the accompanying *t*-test were used as an indicator of the relative contribution of a predictor in comparison to all other predictors that are tested in the model, independent of entry order.

Possible mediating effects were determined according to the procedure described by Baron and Kenny (1986): when both a predictor and a possible mediator explain significant variance in a dependent variable, the mediator is entered before the predictor in the sequential regression analyses to reveal whether the predictor does not any longer explain significant variance, when taking the influence of the mediator into account. Moderating effects were explored by entering centered interaction terms between the predictor and the moderator in the regression analyses, after controlling for their main effects. Due to the relatively large number of explorative tests performed in these analyses, a more conservative threshold of $p < 0.001$ was used. To control for possible confounding effects of medication, Pearson correlation coefficients were calculated between the use and duration of every medication strategy prescribed at the time of diagnosis and changes in anxiety and depressed mood at the 3- and 5-year follow-ups. In the event of a significant correlation, the effects of the medication strategy was taken into account by entering the medication strategy at step 2 before the stress-

vulnerability factors in the regression analyses. Statistical analyses were all conducted with SPSS/Windows 9.0 with a minimum of 76 patients sharing complete data sets.

RESULTS

Clinical and Psychological Health Status during the Study Period

Levels of clinical status (disease activity, functional disability, and pain) and psychological distress (anxiety and depressed mood) when entering the study were comparable to those previously reported in representative samples with recent or longstanding RA (Huiskes et al., 1990a; Meenan et al., 1991; Evers et al., 1998b) (see Table 1 for means and SDs of clinical status and psychological distress levels during the study period).

During the 5-year period, there was a significant improvement in clinical status. Both indicators of disease activity, pain and one of the functional disability measures, grip strength, significantly decreased within 5 years after diagnosis ($F(3,73) = 22.2$, $p < 0.001$ for ESR; $F(3,73) = 10.6$, $p < 0.01$ for the joint score; $F(3,75) = 9.6$, $p < 0.01$ for pain; $F(3,75) = 14.5$, $p < 0.001$ for grip strength). Posthoc tests indicated that this improvement in clinical status was most obvious in the first year of the disease: all indicators decreased in this year ($t = 3.06$, $p < 0.01$ for ESR; $t = 3.25$, $p < 0.01$ for the joint score; $t = 2.20$, $p < 0.05$ for pain; $t = 4.29$, $p < 0.001$ for grip strength) (Evers et al., 1997), possibly due to the beneficial effects of medication (van Jaarsveld et al., 2000; van Everdingen et al., 2002). After the first year of the disease, clinical status remained relatively stable, as indicated by nonsignificant posthoc tests between 1 and 3 years and between 3 and 5 years, with one exception: ESR significantly decreased further between 1 and 3-year follow-up ($t = 3.11$, $p < 0.01$), but not between 3 and 5-year follow-up. In contrast to the considerable improvement in clinical status, mean psychological distress remained relatively stable during the study period. Although an overall decrease was found for anxiety during the 5-year study period ($F(3,73) = 4.37$, $p < 0.05$), posthoc tests between the different assessments points were all nonsignificant. In addition, depressed mood did not change significantly during the study period.

Examining risk groups for psychological distress at the different assessment points, 32-39% and 18-26% of the patients scored equal to or higher than the mean scores of psychiatric outpatients on depressed mood and anxiety, respectively, while 17-21% and 12-21% scored equal to or higher than the mean scores of patients with a clinical depression or anxiety diagnosis, respectively (van der Ploeg et al., 1980; Zwart & Spooren, 1982).

Table 1 Means and SDs of Clinical and Psychological Health Status at the Time of Diagnosis and at the 1, 3, and 5-Year Follow-ups in 78 RA Patients

Disease activity and pain	ESR		Joint score		Pain	
	M	SD	M	SD	M	SD
Diagnosis	29.4	22.3	97.5	100.7	15.8	4.9
1-yr. Follow-up	23.6	22.4	66.7	75.7	14.6	5.4
3-yr. Follow-up	17.7	13.2	63.4	90.4	14.0	5.6
5-yr. Follow-up	20.0	14.7	73.1	110.6	13.7	5.3

Functional disability [a]	Grip strength		Mobility		Self-care	
	M	SD	M	SD	M	SD
Diagnosis	32.2	22.0	19.5	6.1	24.2	5.9
1-yr. Follow-up	40.2	26.0	21.1	5.8	25.1	5.7
3-yr. Follow-up	43.1	24.4	20.9	6.4	25.9	6.1
5-yr. Follow-up	41.9	24.8	20.3	6.6	25.1	6.5

Psychological distress	Anxiety		Depressed mood	
	M	SD	M	SD
Diagnosis	18.75	6.23	3.72	4.76
1-yr. Follow-up	18.75	6.91	3.16	4.15
3-yr. Follow-up	18.07	5.39	3.32	4.08
5-yr. Follow-up	17.46	6.16	2.84	4.08

[a] Lower levels of grip strength, mobility and self-care indicate higher levels of functional disability.

Predictors of Anxiety and Depressed Mood at the 3 and 5-Year Follow-ups

Correlations between stress-vulnerability factors at the time of diagnosis and change of anxiety and depressed mood at the 3 and 5-year follow-ups are presented in Table 3. Results indicated that the personality dimension of neuroticism was significantly related to an increase in depressed mood at both assessment points and an increase in anxiety at the 5-year follow-up. Moreover, a worse clinical status was related to an increase in psychological distress: higher levels of disease activity and functional disability were associated with an increase in anxiety at the 5-year follow-up, and higher levels of functional disability were related to an increase in depressed mood at the 3 and 5-year follow-ups. Nonsignificant correlations were revealed between changes in anxiety and depressed mood at both

Table 2 Correlations at the Time of Diagnosis

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Demographic variables																
1. Age																
2. Sex	.08															
3. Educational level	-.40***	-.31**														
4. Marital status	-.03	-.18	.09													
Personality characteristics																
5. Neuroticism	.00	.21	-.11	-.12												
6. Extraversion	-.13	-.15	.01	.10	-.35**											
Clinical status																
7. Disease activity	-.16	.18	.02	.00	.18	.00										
8. Functional disability	.07	.38**	-.11	.05	.37***	-.03	.46***									
9. Pain	-.26*	-.14	.17	.10	.14	.04	.45***	.21								
Psychological stressors																
10. Disease impact	-.03	.20	-.05	-.21	.43***	-.15	.30**	.41***	.32**							
11. Major life events	-.28*	-.06	.31**	.00	.34**	.01	.02	.02	.22	.22						
Coping																
12. Active probl.-focusing	-.33*	-.32**	.44***	.14	-.18	.26*	-.05	-.25*	.08	-.12	.22					
13. Passive avoidance	.10	.13	-.02	-.06	.32**	-.23*	.13	.01	.19	.11	.05	.06				
Social Support																
14. Social network	-.08	-.30*	.13	.14	-.18	.24*	.12	-.16	.00	-.08	-.12	.26*	.08			
15. Perceived support	-.16	-.10	.10	.16	-.17	.03	.04	-.02	.03	-.02	-.19	.24*	-.02	.26*		
Psychological distress																
16. Anxiety	.00	.25*	-.03	-.20	.74***	-.40***	.16	.26*	.30**	.55***	.40***	-.11	.28*	-.28*	-.24*	
17. Depressed mood	.04	.13	-.10	-.14	.64***	-.31**	.19	.17	.43***	.51***	.20	-.18	.25*	-.24*	-.22*	.75***

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$.

assessment points and the initial assessment of extraversion, pain, disease impact on daily life, major life events, coping, and social support. In addition, demographic variables of age, sex, and marital status were not related to changes in anxiety or depressed mood at follow-up assessments. However, lower education level was significantly related to an increase in anxiety and depressed mood at the 5-year, but not at the 3-year follow-up.

Multiple regression analyses were then performed to study the relative contribution of the stress-vulnerability factors for long-term changes in psychological distress. Anxiety and depressed mood at the 3 and 5-year follow-up were used as dependent variables. In the first step, the initial assessments of anxiety and depressed mood at the time of diagnosis were entered, followed by the stress-vulnerability factors that were significantly related to changes in anxiety or depressed mood at at least one assessment point: education level, neuroticism and two indicators of clinical status (disease activity and functional disability), all measured at the time of diagnosis. As Table 4 reveals, results showed that lower education level significantly predicted anxiety at the 3 and 5-year follow-ups and depressed mood at the 5-year follow-up (Fchange = 4.80, $p < 0.05$ and Fchange = 10.00, $p < 0.01$ for anxiety at the 3 and 5-year follow-ups, respectively; Fchange = 5.71, $p < 0.05$ for depressed mood at the 5-year follow-up), after taking into account the effects of initial levels of psychological distress in the first step (Fchange = 54.32, $p < 0.001$ and Fchange = 31.04, $p < 0.001$ for anxiety at the 3- and 5-year follow-up, respectively; Fchange = 44.61, $p < 0.001$ and Fchange = 23.10, $p < 0.001$ for depressed mood at the 3 and 5-year follow-up, respectively). Neuroticism at step 3 explained significant additional variance to anxiety and depressed mood at the 3 and 5-years follow-ups (Fchange = 4.45, p < 0.05 and Fchange = 10.28, $p < 0.01$ for anxiety at the 3- and 5-year follow-ups, respectively; Fchange = 20.90, $p < 0.001$ and Fchange = 13.87, $p < 0.001$ for depressed mood at the 3 and 5-year follow-ups, respectively), while clinical status at step 4 failed to predict additional variance in both measures of psychological distress. As presented in Table 4, beta coefficients for the full regression equation showed that lower education level significantly predicted more anxiety and depressed mood at the 5-year follow-up (t = -2.83; $p < 0.01$ and t = -2.27, $p < 0.05$, respectively). However, neuroticism proved to be the better predictor for depressed mood at the 3 and 5-year follow-ups (t = 4.19, $p < .001$ and t = 3.26, $p < 0.01$, respectively) as well as for anxiety at the 5-year follow-up (t = 2.77, $p < 0.01$). In addition, neuroticism tended towards significance in the prediction of anxiety at the 3-year follow-up (t = 1.77, p = 0.08).

Results were very similar when the entry order of predictor variables was changed. Education level and neuroticism significantly predicted the same indicators of psychological distress, independently of entry order, except that education level only tended to predict anxiety at the 3-year follow-up, when entered after neuroticism or clinical status at step 3 or 4 (Fchange = 3.55, p = 0.06

at step 3 and *F*change = 3.28, $p = 0.07$ at step 4). Similarly, when entering clinical status at step 2 or 3 in the regression analyses (before education level or neuroticism), it still failed to predict significant variance in anxiety at the 3-year follow-up and depressed mood at the 3 and 5-year follow-up. However, clinical status significantly predicted anxiety at the 5-year follow-up, when entered at step 2 or 3 (*F*change = 3.98, $p < 0.05$ at step 2 and *F*change = 3.79, $p < 0.05$ at step 3), indicating that education level and neuroticism both accounted for the relationship between clinical status and anxiety at the 5-year follow-up. Separate analyses for both indicators of clinical status showed that neuroticism and education level only explained the variance of functional disability to anxiety at the 5-year follow-up. The effect of disease activity on anxiety at the 5-year follow-up still remained significant taking into account the effects of education level and neuroticism (*F*change = 4.27, $p < 0.05$), indicating that disease activity was an additional independent predictor of anxiety at the 5 year-follow-up.

Moderator effects were then explored by entering centered interaction terms between all stressors and vulnerability factors in the regression analyses, after controlling for their main effects. Results indicated that none of the interaction terms predicted anxiety or depressed mood at the 3 and 5-year follow-up.

Confounding Effects of Medication

Correlations between the medication strategies prescribed at the time of diagnosis (NSAID alone, NSAID in combination with methotrexate, intramuscular gold, hydroxychloroquine, or prednisone) and changes in anxiety and depressed mood at the 3 and 5-year follow-up indicated that the use and duration of the various medication strategies were not significantly related to changes in anxiety at the 3 and 5-year follow-ups or to changes in depressed mood at the 5-year follow-up. The only significant associations were those between two medication strategies and changes in depressed mood at the 3-year follow-up: the use and duration of intake of hydroxychloroquine were related to an increase, and the use and duration of intake of prednisone were related to a decrease of depressed mood at the 3-year follow-up ($r = 0.33$, $p < 0.01$ and $r = 0.37$, $p < 0.001$ for the use and duration of hydroxychloroquine, respectively; $r = -0.29$, $p < 0.05$ and $r = -0.29$, $p < 0.05$ for the use and duration of prednisone, respectively). However, when controlling for these variables in the regression analysis (Table 4) by entering these medication strategies at step 2 in the regression analyses, neuroticism still significantly predicted depressed mood at the 3-year follow-up (*F*change = 11.75, $p < 0.001$), after controlling for the baseline levels of depressed mood (*F*change = 42.52, $p < 0.001$) and the effects of the medication strategies (*F*change = 4.29, $p < 0.01$). In addition, beta coefficients indicated that neuroticism remained the best predictor of depressed mood at the 3-year follow-up (beta = 0.41; $t = 3.48$, $p < 0.001$) together with the only other significant predictor, the baseline level of depressed mood (beta = 0.32, $t = 2.84$, $p < 0.01$).

Table 3 Correlations between Stress-Vulnerability Factors at the Time of Diagnosis and Change in Anxiety and Depressed Mood after 3 and 5 Years [a]

	Change in anxiety		Change in depressed mood	
	3 yrs.	5 yrs.	3 yrs.	5 yrs.
Demographic variables				
Age	.05	.12	.03	.12
Sex	.04	.09	.17	.13
Educational level	-.22	-.34**	-.17	-.27*
Marital status	.02	.02	.06	.05
Personality characteristics				
Neuroticism	.20	.27*	.39**	.33**
Extraversion	-.07	-.05	-.08	-.10
Clinical status				
Disease activity	.11	.23*	.18	.19
Functional disability	.20	.28*	.25*	.28*
Pain	.10	-.09	-.04	-.04
Psychological stressors				
Disease impact	.15	.00	.17	.18
Major life events	-.12	-.07	.09	.09
Coping				
Active problem-focusing	-.11	-.10	.08	-.11
Passive avoidance	.12	.10	.21	.03
Social support				
Perceived support	-.09	-.08	-.04	-.06
Social network	.10	.00	.02	-.07

[a] Positive scores indicate that stress-vulnerability factors are related to an increase in anxiety and depressed mood.
* $p < 0.05$ ** $p < 0.01$.

DISCUSSION

A comprehensive set of stressors and vulnerability factors was examined at the time of diagnosis for its ability to predict long-term anxiety and depressed mood in patients with RA. Results revealed that a worse clinical status, more neuroticism and lower education level at the time of diagnosis were all related to an increase in indicators of psychological distress after 3 and 5 years, demonstrating that both disease-related stressors and psychosocial vulnerability factors can affect long-term distress in patients with early RA. However, neuroticism proved to be the most consistent and effective predictor, reflecting that this relatively stable personality dimension has the best prognostic value for long-term distress susceptibility in patients, irrespective of biomedical variables, use of medication, or other stressors and vulnerability factors.

Table 4 Multiple Regression Analyses Predicting Anxiety and Depressed Mood at the 3 and 5-year Follow-ups from Stress-Vulnerability Factors at the Time of Diagnosis [a]

	Anxiety				Depressed mood			
	3 yrs.		5 yrs.		3 yrs.		5 yrs.	
	ß [b]	Δ R^2 [c]	ß	Δ R^2	ß	Δ R^2	ß	Δ R^2
Psychological distress								
Anxiety	.44**	.42**	.21	.30**				
Depressed mood					.26*	.38**	.15	.24**
Demographic variables								
Educational level	-.16	.04*	-.24**	.08**	-.10	.01	-.21*	.05*
Personality characteristics								
Neuroticism	.24	.03*	.37**	.08**	.48***	.14***	.42**	.12***
Clinical status		.01		.04		.02		.02
Disease activity	.03		.14		.12		.13	
Functional disability	.08		.10		-.01		-.06	
Total Δ R^2		.50***		.50***		.55***		.43***

[a] Selection criterion for the inclusion of stress-vulnerability factors in the regression analyses was a significant correlation with changes in psychological distress at at least one follow-up assessment point (see Table 3).
[b] Probability level of *t*-test.
[c] Probability level of *F*-change.
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$.

The predictive value of neuroticism for future distress levels is well documented in the general population (Clark et al., 1994). Neuroticism also prospectively predicted daily mood disturbances in patients with RA (Affleck et al., 1992), suggesting, together with our findings, that this relatively stable personality characteristic has prognostic value for short and long-term psychological distress in patients with RA. Independently from neuroticism, a lower level of education predicted anxiety at the 3 and 5-year follow-up and depressed mood at the 5-year follow-up. As for neuroticism, the prognostic value of lower socioeconomic status on future distress is well established in the general population (Dohrenwend, 1990) and concurrent and prospective links have also been reported in patients with RA (Hawley & Wolfe, 1988; Berkanovic et al., 1996; Brekke et al., 1999). Irrespective of whether individuals are confronted with a long-term chronic condition, such as RA, distress levels seem to be similarly affected by the relatively stable personality characteristic of neuroticism and education level. In contrast, the relationship of clinical status to future distress did not remain significant in regression analyses, except for anxiety levels at the 5-year follow-up. Detailed analyses also revealed that both neuroticism and education level accounted for the relationship of functional disability to anxiety at the 5-year follow-up, but not that of disease activity to anxiety at the 5-year follow-up. These results are in accord with previous findings showing that individuals with higher neuroticism scores and lower education levels are more disabled and complain more about physical symptoms, while their biomedical status of disease activity is about the same (Costa & McCrae, 1987; Watson & Pennebaker, 1989; Berkanovic et al., 1996; Brekke et al., 1999). Consequently, reasons other than RA disease activity, such as a lack of health behaviors and perceptions of control or more selective processing of bodily signals (Larsen, 1992; Pincus & Callahan, 1995; Brekke et al., 1999), may account for the relationship between the physical symptoms reported and future distress. Together, these findings strongly suggest that RA itself has relatively little, if any, effects on the long-term course of psychological distress, and whether individuals become more depressed or anxious in the long run is determined by relatively general and stable vulnerability factors.

Although vulnerability factors for psychological distress found in our study seem to correspond closely to those in the general and psychiatric populations, this does not necessarily imply that neuroticism and education level act in the same way in patients with RA as in controls. Indeed, research has revealed specific, disease-related mediators in patients with RA for both vulnerability factors. For example, the relationship between lower education level and mortality rates in patients with RA has been shown to be mediated by an attitude of helplessness toward the disease (Callahan et al., 1996), while the relationship of neuroticism to future pain reports could be explained by the tendency of patients to catastrophize when faced with pain (Affleck et al., 1992). These findings suggest that links of neuroticism and education level to future outcomes might be differently

determined in patients with RA than in the general population, at least with regard to physical outcomes. Perhaps even more important, these results also indicate that their effects are mediated by actual cognitive and behavioral responses to the disease, which can be modified by psychosocial interventions. It may be crucial in future research to specify the physiological, cognitive-emotional, behavioral, and social mechanisms, in terms of how these factors operate when people are faced with a chronic disease and how they affect RA patients' physical and psychological outcomes.

Investigating stress-vulnerability factors at the time of diagnosis enables risk factors to be identified in an early stage of RA. However, some possible limitations of the study should be recognized. Prospective research is inherently threatened by aspects of internal validity, and other unmeasured biomedical or psychosocial factors may account for the relationship to long-term distress. In addition, the generalizability of our findings might be limited due to some selection bias. All patients took part in a long-term clinical trial. Dropouts were also more distressed and scored higher on neuroticism than patients who completed all assessment points, possibly limiting the generalizability of our findings to patients with RA who are only moderately distressed. However, this finding may also be interpreted as further evidence of the role neuroticism plays in psychological distress and may even have led to an underestimation of its effect on long-term distress.

Irrespective of these limitations, the relative strength of the effects found, particularly for the personality characteristic of neuroticism, underline the importance of paying close attention to factors other than RA when studying risk factors for heightening distress over time. In addition, screening for patients with lower education levels and higher levels of neuroticism may be highly recommended in clinical practice, since these patients are known to report physical symptoms that do not stem purely from RA disease activity. Consequently, they may benefit more from educational and multidisciplinary treatments than pharmacological treatment alone. While multidisciplinary treatments have been shown to be possibly effective in RA (Keefe & van Horn, 1993; Hawley, 1995), narrowly focusing on individual variability in these vulnerability factors may considerably improve their effects on long-term physical and psychological outcomes.

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3

3.2 Illness Cognitions

Beyond unfavorable thinking: The Illness Cognition Questionnaire for chronic diseases

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ABSTRACT

The literature on chronic diseases recognizes the role of illness cognition as a mediator between stress and illness. Few conceptualizations and instruments, however, give an indication of both unfavorable and favorable ways of adjusting to an uncontrollable long-term stressor, such as a chronic disease. The authors propose three generic illness cognitions that reflect different ways of reevaluating the inherently aversive character of a chronic condition: helplessness as a way of emphasizing the aversive meaning of the disease, acceptance as a way to diminish the aversive meaning, and perceived benefits as a way of adding a positive meaning to the disease. A self-report instrument, the Illness Cognition Questionnaire, was developed to assess these cognitions across different chronic diseases. The results support the reliable and valid assessment of these illness cognitions in patients with rheumatoid arthritis and multiple sclerosis and indicate the maladaptive function of helplessness and the adaptive function of acceptance and perceived benefits for the long-term physical and psychological health of patients with a chronic disease.

INTRODUCTION

In recent decades, the role of cognition has been extensively recognized in the development, maintenance, and modification of emotional disorders and psychological well-being (e.g., Beck et al., 1979; Bower, 1981; Lang, 1984). Health psychologists have extended this line of research to the impact of health-related cognitions on physical health and disease outcomes, largely stimulated by stress-illness and self-regulatory approaches (Lazarus & Folkman, 1984; Leventhal et al., 1984). In this tradition, it has been commonly assumed that illness cognitions are an important mediator between disease and patients' well-being and that the way patients perceive and think about their diseases accounts for much of the individual differences in their physical and psychological health status.

A main focus of attention has been the structure of illness cognitions when patients are faced with a chronic disease - by definition, an inherently aversive, long-term condition with a relatively high degree of uncontrollability and unpredictability. Various empirical approaches have identified multidimensional patterns of illness cognitions and provided a better understanding of possible cognitive reactions to long-term stress (e.g., Leventhal & Nerenz, 1985; Turk et al., 1986; Weir et al., 1994; Weinman et al., 1996; see also Scharloo & Kaptein, 1997). However, evidence of the generic structure across different populations (e.g., Schiaffino & Cea, 1995; Heijmans & de Ridder, 1998) and consistent prediction of future health status is rare (e.g., Stanton & Snider, 1993; Schiaffino et al., 1998; Pakenham, 1999). Instead, constructs broadly related to the concept of control, such as helplessness, hopelessness, and cognitive distortion, have most consistently been found to predict unfavorable long-term outcomes in various chronic diseases (e.g., Greer et al., 1990; DeVellis & Blalock, 1992; Smith et al., 1994; Everson et al., 1996; Parle et al., 1996) suggesting that individual differences in adjusting to long-term stress can largely be explained by a single dimension of maladaptive thinking.

Consistent with the supposed independence of positive and negative affect systems (e.g., Costa & McCrae, 1980; Watson & Tellegen, 1985), preliminary evidence indicates that assessing positive in addition to negative cognitions enhances the predictability of outcomes, such as depression (e.g. Kendall et al., 1989), suggesting that both adaptive and maladaptive cognitions may be crucial to fully understanding individual differences in adjusting to chronic diseases. However, the role of possible adaptive cognitions has received far less attention, and there is a general lack of cognitive dimensions demonstrating consistently beneficial and health-promoting effects (see Gillham & Seligman, 1999). For example, although the lack of perceived control has generally been demonstrated to be maladaptive, perceived control does not appear consistently beneficial and can adversely affect well-being in uncontrollable situations, like disease flare-ups (e.g., Schiaffino et al., 1991; Tennen et al., 1992; Newsom et al., 1996; Helgeson, 1999).

This lack of uniform effects of factors assumed to be adaptive has been frequently ascribed to the complexity of adaptive processes in highly uncontrollable situations (e.g., Averill, 1973; Silver & Wortman, 1980; Thompson et al., 1988; Smith et al., 1997). However, recent theoretical approaches have focused more on the cognitive reevaluation of the stressor as a necessary component of successfully adjusting to reduce adverse effects, without controlling the stressor per se (e.g., Rothbaum et al., 1982; Brandtstaedter & Renner, 1992; Thompson et al., 1994; Heckhausen & Schulz, 1995).

Considering that evaluative processes, in terms of the meaning ascribed to the event, are inherent to adjusting to long-term stress, maladaptive and adaptive processes might be relatively uniformly described as cognitive reevaluations of the stressor. In relation to positive-negative valence, three types of reevaluations can be distinguished when one is faced with long-term stress: (1) cognitions that emphasize the negative meaning of the stressor (e.g., with an attitude of helplessness or hopelessness), (2) cognitions that diminish the aversive meaning of the stressful event (e.g., by accepting the negative impact of the stressor and learning to live with it), and (3) cognitions that add a positive meaning to the event (e,g, by focusing on additional positive consequences of the stressor). This conceptualization of positively and negatively valenced cognitions, reflecting dimensions of increased negative, decreased negative, and increased positive thinking when one faces long-term stress (see also Kendall, 1992), may provide a comprehensive pattern of cognitive adjustment that can uniformly predict the long-term health status of patients with chronic diseases.

Emphasizing the negative meaning entails focusing on the adverse aspects of the disease as an uncontrollable, unpredictable, and unchangeable condition and generalizing these consequences to daily functioning. This kind of cognitive reaction has been described in helplessness-hopelessness theory as a negative explanatory style when faced with a stressful event (Seligman, 1975; Abramson et al., 1978, 1989), consisting of negative outcome expectancies, global and stable attributions ascribed to the event, and inferred negative characteristics ascribed to the self. Considerable research has demonstrated the prominent role of helplessness-hopelessness constructs, indicating that they are a prospective risk factor for an unfavorable physical and psychological health status in various chronic diseases (e.g., Greer et al., 1990; DeVellis & Blalock, 1992; Smith et al., 1994; Everson et al., 1996; Parle et al., 1996).

In contrast, the aversive meaning of the disease can also be diminished by patients' acknowledging that they are chronically ill and simultaneously perceiving the ability to live with and master the consequences of their disease. This cognition has previously been described in terms of acceptance (see e.g., Hayes et al., 1994; McCracken, 1998). Acceptance means recognizing the need to adapt to a chronic illness while perceiving the ability to tolerate the unpredictable, uncontrollable nature of the disease and handle its averse consequences. The possible beneficial

function of this cognition has been supported by concurrent associations with a more favorable physical and psychological health status in various chronic conditions (e.g., Revenson & Felton, 1989; Summers et al., 1991; Li & Moore, 1998; McCracken, 1998). Prospective studies have also provided preliminary evidence for beneficial long-term effects of this cognition on psychological health in patients with cancer and multiple sclerosis (Brooks & Matson, 1982; Carver et al., 1993).

One can also add a positive meaning to the disease by perceiving additional positive consequences of the stressful condition. A perception of benefits has been frequently reported as a reaction to highly uncontrollable and stressful life events and to confronting loss (for overviews, see Affleck & Tennen, 1996; Tedeschi & Calhoun, 1996; Park, 1997). Three major benefits seem applicable to most patients: changes in life priorities and personal goals, positive personality changes, and strengthened personal relationships. Aside from preliminary evidence from cross-sectional studies, prospective studies on rheumatoid arthritis patients and heart attack victims have supported the adaptive, long-term impact of perceived benefits on psychological and physical health indicators (Affleck et al., 1987; Tennen et al., 1992).

The concepts of helplessness, acceptance and perceived benefits have been studied for various chronic diseases, and findings give preliminary evidence of generic, long-term effects on physical and psychological well-being. However, various instruments have been used to assess these concepts, measuring them as disease-specific cognitions or as traitlike constructs unrelated to chronic illnesses. For example, helplessness has been assessed with disease-specific scales for various chronic diseases (e.g., Nicassio et al., 1985; Watson et al., 1988; Flor et al., 1993) or with traitlike measures of general helplessness-hopelessness constructs (e.g., Beck et al., 1974; Millon et al., 1982). Similarly, acceptance has been assessed with disease-specific scales for patients with disabilities, chronic pain or HIV (e.g., Linkowski, 1972; Felton & Revenson, 1984; Thompson et al., 1994; McCracken, 1998), and with general coping questionnaires (e.g., Carver et al., 1989). Self-report instruments for assessing perceived benefits have been developed for patients with chronic pain (Tennen et al., 1992) and for individuals experiencing severe stress or trauma (Park et al., 1996; Tedeschi & Calhoun, 1996). So far, we know of no instrument that measures these constructs as generic illness cognitions across chronic diseases.

The object of our study was to develop a short, reliable, valid questionnaire for assessing the a priori constructs of helplessness, acceptance, and perceived benefits in patients with chronic diseases. We intended to identify a basic set of illness cognitions applicable across a range of chronic diseases that indicate both unfavorable and favorable ways of adjusting to chronic diseases. For this purpose, we developed the Illness Cognition Questionnaire (ICQ) in a sample of rheumatoid arthritis (RA) patients, and we cross-validated the factor structure in a sample of

multiple sclerosis (MS) patients. Test-retest reliability was assessed in subsamples of these groups. We hypothesized that three relatively distinct, reliable, and stable dimensions of the a priori illness cognitions would emerge from both patient groups. In addition, we examined concurrent validity by studying relationships between the ICQ scales and constructs assumed related to illness cognitions in stress-illness approaches, such as physical and psychological health outcomes, process measures of coping and social support, and two basic personality dimensions of the Big Five - neuroticism and extraversion - that have been demonstrated to be most significant for health and well-being. On the basis of theoretical and empirical literature indicating that helplessness is relatively closely related to unfavorable physical and psychological health status, moderately to closely related to more neuroticism and less extraversion, and weakly to moderately related to more passive coping and less social support (e.g., Costa & McCrae, 1980; Nicassio et al., 1985; DeVellis & Blalock, 1992; Smith & Wallston, 1992; Smith et al., 1994; Everson et al., 1996; Shnek et al., 1997), we expected similar relationships to support this scale's concurrent validity. In contrast, relatively opposite relationships provide evidence for the concurrent validity of acceptance and perceived benefits (e.g., Affleck et al., 1987; Revenson & Felton, 1989; Summers et al., 1991; Tennen et al., 1992; Carver et al., 1993; Affleck & Tennen, 1996; Li & Moore, 1998; McCracken, 1998). To obtain preliminary evidence for discriminant validity between cognitions assumed to be adaptive and maladaptive, we expected acceptance and perceived benefits to demonstrate the closest associations to positive outcome, personality, and process measures, such as positive mood, optimism, and active coping (e.g., Costa & McCrae, 1980; Watson & Tellegen, 1985; Zautra et al., 1995; Affleck & Tennen, 1996; Park et al., 1996; Smith & Christensen, 1996), and we expected that the significance of these effects would continue when we controlled for their negative counterparts (i.e., negative mood, pessimism, and passive coping). Moreover, we prospectively investigated the predictive validity of ICQ scales for the long-term health status of RA and MS patients, hypothesizing that helplessness would be related to deterioration of patients' physical and psychological health status, and acceptance and perceived benefits to improvement. To obtain additional support for the generic character of the illness cognitions, we expected all relationships to be relatively uniform in both RA and MS patients and unaffected by the type of chronic disease. Finally, because the specificity of health-related constructs has been questioned insofar as they reflect aspects of neuroticism or negative affectivity (Costa & McCrae, 1980; Watson & Pennebaker, 1989; McCrae, 1990), particularly in relation to positive personality, outcome, or process measures (e.g., Funk & Houston, 1987; Smith et al., 1989; Green et al., 1999), we controlled for confounding effects of neuroticism in all correlational analyses.

METHODS

Generation of Items and Scale Development of the ICQ

On the basis of the proposed conceptualization of illness cognitions, an item pool was generated, consisting of newly constructed items and items from existing inventories that were revised slightly to assess illness cognitions (Linkowski, 1971; Felton & Revenson, 1984; Nicassio et al., 1985; Carver et al., 1989; Tennen et al., 1992). All items had to meet the following scale construction criteria: be positive and unidirectionally formulated in simple, clear language, contain less than 20 words, be unambiguous and relevant to the proposed construct, and contain a direct link between the person and the illness. Respondents were asked to indicate on a 4-point Likert scale the extent to which they agree with a list of statements by people with a long-term illness (1 = not at all, 2 = somewhat, 3 = to a large extent, 4 = completely). The following instruction was used: 'On the next page is a list of statements by people with a long-term illness. Please indicate the extent to which you agree with these statements by circling one of the answers following the statement. Do not spend too much time considering your answer. Your first impression is usually the best.' Then, an example of how to respond to these statements was given.

The item pool was judged on the basis of relevance and comprehensibility by several researchers or health care professionals working with patients having a wide range of chronic diseases. Subsequently, interviews were conducted with patients with different chronic diseases who again evaluated the relevance and comprehensiveness of the items. Forty-five items were then selected for future research. This initial pool was administered to the RA patients described below. Results indicated that none of the items had to be eliminated because of skewed distributions (skewness and kurtosis < 1). An exploratory principal-components factor analysis with oblique rotation was then performed with the 45-item version of the questionnaire. The scree test indicated that a 3-factor solution was preferable. Items with a loading above .65 and a difference in loading to the secondary factors of .40 or more were retained. Twenty-three items met this criterion. In addition, 5 items were discarded because of overlapping contents, resulting in 18 ICQ items.

Patients and Procedures

Participants were 263 outpatients with RA from seven participating hospitals and 167 patients with MS seeking treatment in one of two MS outpatient clinics in the Netherlands. Inclusion criteria for RA were a minimum age of 18 years and a diagnosis of RA according to American College of Rheumatology (ACR) criteria (Arnett et al., 1988). The RA sample was predominantly female (66%) and married (78%) with at least a primary educational level (an average of 7 years of formal education) or a secondary educational level (an average of 11-13 years of formal

education) (25% and 64%, respectively). The mean age was 58.1 years (SD 13.6, range 20-85). Mean time since diagnosis was 10.3 years (SD 9.7, range 0-54). Inclusion criteria for the MS sample were a minimum age of 18 years and a diagnosis of MS according to the revised criteria for definite MS (Poser et al., 1983). The total group involved 89 relapsing remitting, 68 secondary progressive, 3 relapsing progressive, and 7 primary progressive patients. Most of the participants were female (67%) and married (81%) and had a secondary educational level (2% primary and 70% secondary). The mean age was 40.6 years (SD 8.8, range 21-67). Mean time since diagnosis was 9.4 years (SD 5.9, range 0-29). In comparison to the RA patients, the MS patients were younger ($t(428) = -16.15$, $p < 0.001$) and had a higher educational level ($t(428) = 8.07$, $p < 0.001$); there were no differences with regard to gender, marital status, or duration of disease.

To examine the temporal stability of the instrument, we administered the questionnaire twice to a subsample of 81 RA patients and 67 MS patients, with a 1-year time interval. Although a 1-year time interval is rather long for analyzing test-retest reliability, the scales are supposed to reflect long-term adjustment and were expected to be relatively stable within one year. Patients from these subsamples took part in a long-term follow-up study and had a relatively long duration of disease (> 7 years). Besides the differences in disease duration ($t(261) = 9.47$, $p < 0.001$; $t(165) = 4.25$, $p < 0.001$, for RA and MS, respectively), the MS patients in this subsample were also older than in the original sample ($t(165) = 2.42$, $p < 0.05$); there were no differences with regard to gender, marital status, or educational level.

For studying concurrent validity, subsamples of 208 RA patients and 134 MS patients from the original samples were randomly selected. Clinical and self-report measures of physical and psychological health, personality dimensions, coping, and social support were simultaneously administered to these patients with the ICQ. When possible, the same instruments were used in the two samples to allow comparisons of the relationships between different chronic diseases. An exception was the disease-specific measurement of the most prominent physical complaints, that is, pain in RA patients and fatigue in MS patients. In addition, disease-specific measures of disease activity were collected in randomly selected subsamples (106 RA patients and 88 MS patients). To study predictive validity, we again compield the physical and psychological health status outcome measures one year later in randomly selected subsamples of 95 RA and 100 MS patients.

Measures

Disease activity was assessed in the RA sample by clinical joint score ratings (number of swollen and painful joints; Fuchs et al., 1989). In the MS sample, disability was scored by a neurologist on the basis of Kurtzke's (1983) expanded

disability status scale. A standardized composite score of these disease-specific measures was used as a common indicator of disease activity.

Functional disability was assessed in both samples with a composite score on the Mobility and Self-Care scale of the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL; Huiskes et al., 1990a; Evers et al., 1998b), a questionnaire derived from the AIMS, which was originally developed to assess various aspects of physical, psychological, and social health in arthritis patients. Previous research showed reliability and validity of the IRGL scales to be highly satisfactory in RA patients (Huiskes et al., 1990a; Evers et al., 1998b), and the instrument from which it was derived, the Arthritis Impact Measurement Scales (AIMS), has also been shown to be reliable and valid for use in MS patients (Schiaffino et al., 1996, 1998). Items of the IRGL scales are scored on a 4 or 5-point Likert scale. The Mobility and Self-care scales assess the functional capacities of the lower and upper extremities in the past month (15 items). Higher scores indicate higher levels of functional disability. Cronbach's alpha for the Functional Disability scale in the present study was 0.98 for RA patients and 0.92 for MS patients.

Physical complaints were assessed by a standardized composite score from the most prominent physical complaint (i.e., pain in RA patients and fatigue in MS patients). Pain was assessed with the IRGL Pain scale (6 items), which measures the severity and frequency of painful episodes and swollen joints and the duration of morning stiffness in the last month. Cronbach's alpha for the Pain scale in the present study was 0.93. Fatigue was assessed with the Fatigue scale (8 items) of the Checklist Individual Strength (CIS; Vercoulen et al., 1996), which measures patients' level of fatigue for the previous two weeks. Cronbach's alpha for the Fatigue scale in the present study was 0.92.

Negative mood was measured in both samples with a standardized composite score on the IRGL Anxiety and Depressed Mood scales. The Anxiety scale is a shortened version of the Dutch State Anxiety Scale (10 STAI items; van der Ploeg, Defares, & Spielberger, 1980), that assesses anxiety level in the past month. The Depressed Mood scale (6 items) is derived from Zwart and Spooren's questionnaire (1982) and assesses various depressed mood states over the previous two weeks. Cronbach's alpha for the Negative Mood scale in the present study was 0.97 and 0.94 in RA and MS patients, respectively.

Positive mood was measured in both samples with the IRGL Positive Mood scale. The Positive Mood scale (6 items) is derived from Zwart and Spooren's questionnaire (1982) and assesses various positive mood states over the previous two weeks. Cronbach's alpha for the scale in the present study was 0.96 and 0.92 in RA and MS patients, respectively.

Disease impact on daily life was measured in both samples by the IRGL Disease Impact scale (10 items), which refers to the general impact the disease has on several areas of daily life (i.e. work, leisure, relationships, sexuality, and

eating). Cronbach's alpha in the present study was 0.96 and 0.89 in RA and MS patients, respectively.

Personality dimensions, that is, neuroticism and extraversion, were measured by a Dutch version of the Eysenck Personality Questionnaire (EPQ; Wilde, 1970; Eysenck & Eysenck, 1991). Optimism and pessimism were measured by a Dutch version of the Life Orientation Test (LOT; Scheier & Carver, 1985). Cronbach's alpha in the present study were 0.85 and 0.89 for neuroticism, 0.81 and 0.83 for extraversion, 0.81 and 0.80 for optimism, and 0.82 and 0.88 for pessimism in RA and MS patients, respectively.

Coping strategies were assessed in both samples with the Utrecht Coping List (UCL; Schreurs et al., 1993), a well documented coping questionnaire in the Netherlands, adopted from Westbrook (1979), which measures active and passive coping strategies when dealing with everyday problems, on a 4-point Likert scale. Active coping was assessed by a composite score on the strategies of problem focusing and comforting cognitions (12 items). Passive coping was measured with the strategy of avoidance (8 items). Cronbach's alpha in the present study was 0.85 and 0.82 for active coping and 0.73 and 0.68 for passive coping in RA and MS patients, respectively.

Social support was measured in both samples with the social functioning scales of the IRGL, which assesses qualitative and quantitative aspects of social support in the past six months, that is, the level of perceived support (5 items) and the size of the social network (number of friends and family members with whom patients associate). Cronbach's alpha for the Perceived Support scale in the present study was 0.98 for RA patients and 0.88 for MS patients.

RESULTS

Principal Components Analysis and Confirmatory Factor Analysis

A principal components factor analysis with oblique rotation was performed in the RA sample. The scree test and the eigenvalues above 1 indicated that a 3-factor solution was preferable, explaining 62% of the total variance. Table 1 shows the items of the 3 factors with the rotated factor loadings in this sample. The factors, labeled according to the a priori constructs as Helplessness, Acceptance and Perceived Benefits, all consisted of 6 items and explained 19%, 34%, and 10% of the variance, respectively. The composition of the factors was completely in accordance with the a priori assignment of items, demonstrating loadings on the a priori factor above .65, with a .40 or greater difference in loading on the secondary factors. The three-factor model for the ICQ items was then tested in the MS sample by using confirmatory factor analyses (AMOS 4.0; Arbuckle, 1994). Two different confirmatory factor analyses were performed, testing an orthogonal and an oblique

Table 1 Principal-Component Factor Analysis with Oblique Rotation in Patients with RA, and Means and Standard Deviations, Cronbach's Alpha and Test-Retest-Reliability in Patients with RA (n=263) and MS (n=167) [a]

	Helplessness	Acceptance	Benefits
15. My illness frequently makes me feel helpless.	**.81**	-.35	-.03
12. My illness limits me in everything that is important to me.	**.81**	-.41	.02
5. My illness controls my life.	**.80**	-.36	.00
1. Because of my illness, I miss the things I like to do most.	**.76**	-.23	-.02
9. My illness prevents me from doing what I would really like to do.	**.76**	-.27	-.03
7. My illness makes me feel useless at times.	**.77**	-.33	-.01
10. I have learned to accept the limitations imposed by my illness.	-.22	**.85**	.34
3. I have learned to live with my illness.	-.30	**.84**	.30
13. I can accept my illness well.	-.34	**.84**	.24
17. I can cope effectively with my illness.	-.39	**.82**	.22
2. I can handle the problems related to my illness.	-.40	**.79**	.29
14. I think I can handle the problems related to my illness, even if the illness gets worse.	-.38	**.73**	.24
4. Dealing with my illness has made me a stronger person.	-.03	.27	**.79**
6. I have learned a great deal from my illness.	.00	.31	**.79**
18. My illness has taught me to enjoy the moment more.	-.04	.27	**.78**
8. My illness has made life more precious to me.	.02	.35	**.75**
16. My illness has helped me realize what's important in life.	-.11	.31	**.71**
11. Looking back, I can see that my illness has also brought about some positive changes in my life.	-.04	.03	**.65**
Means (SD)			
RA	12.66 (4.24)	16.65 (4.20)	15.20 (4.22)
MS	13.44 (4.40)	15.78 (4.37)	15.53 (4.46)
Cronbach's alpha			
RA	.88	.90	.84
MS	.88	.91	.85
Test-retest reliability			
RA	.79	.76	.74
MS	.73	.78	.68

[a] The following items are adjusted from existing scales: items 4, 6, 8 and 16 (Tennen et al., 1992), items 1, 7 and 9 (Felton & Revenson, 1984; Linkowski, 1972), items 5 and 17 (Nicassio et al., 1985), and item 3 (Carver et al. 1989). Factor loadings above 0.60 are in boldface type.

solution. The fit indices consistently indicated a highly satisfactory fit (with fit indices above 0.90) only for the oblique model (χ^2 (132, N=167) = 230.91, p < 0.001; Comparative Fit Index = 0.94; Tucker-Lewis Index = 0.93; Incremental Goodness-of-fit Index = 0.94). When comparing the two models, the oblique model also had a significantly better fit than the orthogonal model (χ^2 *diff* (3, N=167) = 79.02, p < 0.001).

Psychometric Properties

Reliability. Means and standard deviations, Cronbach's alpha, and test-retest reliability for RA and MS patients are presented in Table 1. Cronbach's alpha demonstrated adequate internal consistencies for all scales, ranging from 0.84 to 0.91 in the samples. In addition, Pearson product-moment correlation coefficients between the two measurement points indicated high test-retest reliability for all scales in both samples (all above 0.67).

Intercorrelations among the scales. Intercorrelations between the scales revealed nonsignificant to moderate relationships. Helplessness and Acceptance were moderately negatively correlated in both samples (r = -0.43, p < 0.001; r = -0.45, p < 0.001 for RA and MS patients, respectively), whereas Acceptance and Perceived Benefits were moderately positively correlated (r = 0.36, p < 0.001; r = 0.46, p < 0.001 for RA and MS patients, respectively). The correlation between Helplessness and Perceived Benefits was nonsignificant in the RA sample (r = -0.03, ns), and weakly negative in the MS sample (r = -0.19, p < 0.05).

Relationship to demographic variables and duration of disease. Gender differences were not found between the scales. Nor were the scales significantly related to age and educational level, with the exception of a weak negative correlation between Helplessness and education level in the RA sample (r = -0.23, p < 0.001) and a weak negative correlation between age and Perceived Benefits in the MS sample (r = -0.18, p < 0.05), indicating greater Helplessness for patients with a lower education level in the RA sample and more Perceived Benefits among younger patients in the MS sample. In addition, duration of disease was related to Helplessness in both samples (r = 0.19, p < 0.01; r = 0.20, p < 0.05 for RA and MS, respectively), to Perceived Benefits in the RA sample (r = 0.17, p < 0.01), and when controlling for age, to Perceived Benefits in the MS sample, (r = 0.16, p < 0.05), indicating increased helplessness and perceived benefits for patients with longer duration of disease. Because there is preliminary evidence that cognitive adjustment takes place particularly in the initial years of a chronic disease (e.g., Cassileth et al., 1984; Smith et al., 1997; Evers et al., 1998a), correlations with duration of disease were also calculated for patients with a maximum disease duration of 5 years (123 RA patients and 47 MS patients). Whereas correlations with Helplessness and Perceived Benefits were no longer significant in these

subgroups, significant correlations were found in both samples with Acceptance (r = 0.24, $p < 0.01$; r = 0.30; $p < 0.01$ for RA and MS, respectively), indicating increased acceptance during the initial years of the disease.

Table 2 Correlations and Partial Correlations (Controlling for Neuroticism) between the Illness Cognition Questionnaire Scales and the Criterion Measures of Concurrent Validity in Patients with RA and MS (n=342)

	Helplessness		Acceptance		Benefits	
Criterion measures	r	pr	r	pr	r	pr
Physical health						
Disease activity [a]	.44***	.47***	-.05	-.02	.00	.00
Functional disability	.54***	.54***	-.22***	-.16***	-.01	-.01
Physical complaints [b]	.50***	.38***	-.32***	-.18***	-.21***	-.16***
Psychological health						
Negative mood	.62***	.40***	-.54***	-.33***	-.18**	-.08
Positive mood	-.53***	-.33***	.50***	.33***	.29***	.24***
Disease impact	.64***	.56***	-.36***	-.22***	-.07	.00
Personality dimensions						
Neuroticism	.54***	-	-.47***	-	-.18**	-
Extraversion	-.34***	-.14**	.22***	.03	.16**	.10
Optimism	-.47***	-.26***	.59***	.43***	.39***	.35***
Coping						
Active	-.26***	-.15**	.38***	.30***	.43***	.41***
Passive	.29***	.24***	.03	.14**	.03	.07
Social support						
Perceived support	-.31***	-.20***	.20***	.08	.08	.03
Social network	-.19**	-.14**	.15**	.09	.14*	.11*

[a] Disease activity was assessed in subsamples of 194 patients (106 RA and 88 MS).
[b] The most prominent physical symptom was assessed (i.e. pain in RA and fatigue in MS).
* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$ (two-tailed).

Concurrent Validity

Pearson's correlation coefficients between the ICQ scales and the measures of concurrent validity were first calculated separately for the RA and MS samples. As expected, results demonstrated a very similar pattern in the direction and strength of correlations in both samples. Multiple regression analyses were then performed

to examine possible differences in the relationships between the ICQ scales and the measures of concurrent validity between the two samples. In the first two steps, illness category (RA and MS) and one of the ICQ scales were entered, followed by their centered interaction term in the third step. As anticipated, the interaction between illness category and the scales of the ICQ were nonsignificant for all measures of concurrent validity with one exception: that between illness category and Acceptance for the prediction of functional disability. Separate analyses revealed that Acceptance was significantly related to lower levels of functional disability in RA patients but not in MS patients. Because of the uniform pattern of all other criterion measures in both illness groups, we subsequently calculated correlations for both samples together.

As shown in Table 2, the direction and magnitude of the correlations closely corresponded to hypothesized relations. Illness cognitions of Helplessness were moderately (r = 0.25 - 0.45) to relatively highly (r > 0.45) related to a worse physical and psychological health status, that is, more pronounced levels of disease activity, functional disability and physical complaints, increased negative mood and decreased positive mood, and increased impact of the disease on daily life. In personality dimensions, helplessness was highly related to more neuroticism and less optimism and moderately related to less extraversion. For coping and social support measures, weak to moderate correlations were found with the more frequent use of passive coping, less frequent use of active coping, and less social support.

A nearly opposite pattern emerged for Acceptance. Although correlations with physical health were somewhat lower than for Helplessness, Acceptance was relatively highly related to a better psychological health, less neuroticism, and more optimism. In addition, weak to moderate correlations were found with more extraversion, higher levels of active coping, and more social support. A similar pattern became apparent for Perceived Benefits, although the general strength of the correlations was overall lower than for Acceptance. As expected, Acceptance and Perceived Benefits in particular correlated highly with positive outcome, personality, and process measures (positive mood, optimism, and active coping). This pattern became even more evident when we controlled for their negative counterparts (negative mood, pessimism, and passive coping), as correlations with positive outcome, personality, and process measures were substantially reduced for Helplessness but not for Acceptance and Perceived Benefits. When we controlled for the influence of neuroticism for all measures of concurrent validity, correlations were overall only marginally reduced for the three scales, and most correlations remained significant (see Table 2).

We then performend multiple regression analyses to evaluate the amount of variance explained by the three scales and their relative contribution to the criterion measures. When we entered all predictors together in one model, illness cognitions explained between 5% (for social network) and 45% (for negative mood) of the

variance in the criterion variables. Beta coefficients indicated that Helplessness proved to be a significant predictor for all criterion measures, independent of the effects of Acceptance and Perceived Benefits. Acceptance significantly predicted all indicators of psychological health, the personality dimensions of neuroticism and optimism, and active and passive coping, beyond the effects of Helplessness and Perceived Benefits. Perceived Benefits was ultimately an additional significant predictor for positive mood, optimism, and active coping, when the effects of Helplessness and Acceptance were taken into account.

Table 3 Correlations and Partial Correlations (Controlling for Neuroticism) between the Illness Cognition Questionnaire Scales at First Assessment and the Criterion Measures of Predictive Validity in RA and MS patients (n=195) [a]

	Helplessness		Acceptance		Benefits	
Criterion measures	r	pr	r	pr	r	pr
Change in physical health						
Disease activity [b]	.21*	.08	-.31**	-.20*	.00	.05
Functional disability	.24**	.23**	-.09	-.07	-.09	-.07
Physical complaints [c]	.15*	.09	-.24**	-.20**	-.08	-.05
Change in psychological health						
Negative mood	.05	.05	-.17*	-.09	-.08	-.04
Positive mood	-.13	-.06	.18*	.11	.22*	.19**
Disease impact	.16*	.15*	-.13	-.12	-.07	-.06

[a] Criterion measures of predictive validity were the residual gain scores of the outcome measures. Higher scores indicate an increase in the outcome measure.

[b] Disease activity was assessed in RA patients only.

[c] The most prominent physical symptom was assessed (i.e. pain in RA and fatigue in MS).

* $p < 0.05$ ** $p < 0.01$ (two-tailed).

Predictive Validity

We examined predictive validity by studying the relationships between the ICQ scales at first assessment and change in physical and psychological health within one year. To produce reliable change scores, we regressed the health status measures at first assessment on the health status measures at second assessment, resulting in residual gain scores. Pearson correlation coefficients were then separately computed for RA and MS patients. As in the analyses of concurrent

validity, the relationships between the ICQ scales at first assessment and changes in health status measures revealed a relative uniform pattern for the direction and strength of the correlations. To examine whether these relationships would be different for both samples, we studied the interaction between illness category and the ICQ scales for all criterion measures in a series of multiple regression analyses. The health status measure at first assessment was entered in the first step, followed by illness category (RA and MS) and one of the ICQ scales in steps 2 and 3 and their centered interaction term in step 4. According to the results of the single correlation analyses, the interaction between the ICQ scales and illness category was nonsignificant for all criterion measures with one exception: that between illness category and Perceived Benefits when the impact of the disease on daily life was the dependent variable. Separate analyses for RA and MS patients revealed that benefits significantly predicted a decrease in the impact of the disease on daily life in RA patients but not in MS patients.

Pearson correlation coefficients were then computed between the residual gain scores and the ICQ scales at first assessment for both samples. Although there was hardly any systematic change in physical and psychological health status, as indicated by nonsignificant changes in all outcome measures but one (disease activity), several significant correlations were found for all three scales in the expected direction (see Table 3). Helplessness was primarily related to a deterioration of physical health (i.e. an increase of disease activity, functional disability, and physical complaints) as well as to an increase in the impact of the disease on daily life. Acceptance, in contrast, was related to increases in physical and psychological health status. Significant correlations were found between Acceptance and a decrease in disease activity and physical complaints, a decrease in negative mood, and an increase in positive mood. Finally, Perceived Benefits were related to an increase in positive mood. When we adjusted these correlations for the influence of neuroticism, most correlations remained significant (see Table 3). An exception were the correlations between Helplessness and an increase in disease activity and physical complaints and between Acceptance and a decrease in negative and an increase in positive mood.

Multiple regression analyses were then performed to evaluate the amount of variance explained by the three scales and their relative contribution to long-term health status measures. When we included all illness cognitions in one model, illness cognitions additionally explained between 2% and 9% of variance beyond the considerable variance explained by the baseline values of the outcome variables (between 27% and 75%). Beta coefficients indicated different predictors for all outcome measures. Helplessness significantly predicted an increase in functional disability and an increase in the impact of the disease on daily life. Acceptance predicted a decrease in disease activity, physical complaints, and negative mood. Perceived Benefits predicted an increase in positive mood.

DISCUSSION

A common characteristic of chronic diseases is their inherently threatening nature, as patients are confronted with an incurable long-term condition that imposes multiple limitations on functioning in daily life. Individual differences in long-term adjustment may be explained by different ways of cognitively reevaluating the inherently aversive nature of the disease with constructs such as helplessness, acceptance, and perceived benefits. The development of the ICQ provides a self-report instrument that reliably assesses these cognitions in various chronic diseases and shows both unfavorable and favorable ways for adjusting to a chronic condition.

The applicability of the questionnaire to different patient populations with chronic diseases was indicated by the invariant internal structure in patients with RA and MS, revealing a closely corresponding, reliable, and stable pattern of cognitive reactions to a chronic disease. Analyses of concurrent validity strongly supported the proposed stress-vulnerability approach, in which illness cognitions are related to physical and psychological health, personality dimensions, coping, and social support, and these relationships proved to be relatively independent of the influence of neuroticism. In addition, preliminary evidence for discriminant validity between cognitions assumed to be adaptive and maladaptive was provided by the relatively stronger correlations of acceptance and perceived benefits with positive outcome, personality, and process variables. The corresponding correlations in the two samples further indicate the generic nature of these cognitions in patients with different chronic diseases. In addition, correlations with duration of disease give an initial indication that the scales are sensitive to long-term adjustment in chronic diseases, suggesting increased acceptance in the first years of the disease and increased helplessness and perceived benefits in the longer term. Analysis of predictive validity ultimately indicated the expected maladaptive and adaptive function of cognitions; that is, helplessness was related to unfavorable changes, and acceptance and perceived benefits were related to beneficial changes in physical and psychological health. And again, these relationships were relatively independent of the influence of neuroticism. The uniformity of these relationships in both samples, corresponding to previous findings in a wide range of chronic diseases, additionally supports the generic character of the cognitions. Moreover, the capacity of the scales to predict different outcome measures supports the utility of the multidimensional approach and indicates the distinct function of maladaptive and adaptive cognitions in terms of the long-term outcome in chronic diseases.

According to the conceptualization of illness cognitions, our assessment of helplessness differs slightly from the original helplessness-hopelessness theory, as it directly refers to the aversive consequences of a chronic disease. The advantage of this disease-specific concept of helplessness may correspond to its greater predictive validity for the physical health status. Our results generally support this

assumption, demonstrating that helplessness predicted a deterioration of physical health, particularly an increase in functional disability. In contrast acceptance seemed to have benefits for both physical and psychological health, as demonstrated by a decrease in disease activity, physical complaints, and negative mood. Relationships to increased psychological health have previously been reported in patients with breast cancer and multiple sclerosis (Brooks & Matson, 1982; Carver et al., 1993), whereas even maladaptive relationships between stoic or realistic acceptance and mortality have been reported in AIDS and cancer patients (Greer et al., 1990; Reed et al., 1994). The different relationships are probably due to differences in conceptualization. Acceptance was assessed as a type of resignation in the studies demonstrating maladaptive relationships (Greer et al., 1990; Reed et al., 1994), whereas our conceptualization entails the perceived ability to live with and master the aversive consequences of the disease. Relationships of perceived benefits corresponded most to the hypothesized effects of adaptive process variables on positive outcome measures. As in the cross-sectional analyses, where perceived benefits were most closely related to positive outcome, personality, and process measures, the prospective analyses revealed a beneficial relationship to an increase in positive mood, corresponding to previous prospective findings in rheumatoid arthritis patients and individuals experiencing life stress (Tennen et al., 1992; Park et al., 1996).

Instrument development is an ongoing process requiring multiple studies over time. We have demonstrated some aspects of reliability and validity, but several important psychometric characteristics are missing. One limitation might be that the RA and MS populations studied share various common characteristics. Both conditions have a medically based diagnosis (unlike chronic fatigue syndrome), are in most cases progressive and highly uncontrollable and unpredictable (unlike diabetes), lead to physical impairment and confront patients with multiple losses in daily life (unlike asthma), and are not directly life threatening, consequently requiring long-term adjustment processes to find a way to live with the disease (unlike some forms of cancer). Although our conceptualization was theoretically and empirically founded on common elements in chronic diseases, future research would be warranted in studying psychometric properties in other patient populations with chronic illnesses. In terms of construct validity, we did not assess relationships between the ICQ scales and similar constructs more directly related to perceived control, such as self-efficacy or health locus of control. Previous studies comparing these constructs have suggested that the associations between acceptance and benefits and perceived control constructs vary particularly in the face of highly uncontrollable situations. For example, in RA patients with severe pain, perceived benefits and perceived control have been shown to be related to favorable versus unfavorable changes in subsequent health outcomes, respectively (Tennen et al., 1992). Finally, studies on sensitivity to change by treatment modules are clearly recommended.

What is the additional value of a generic instrument of illness cognitions like the present one? Because it contains adjusted constructs of existing single-dimensional questionnaires, the ICQ can be viewed as an instrument refinement, indicating the multidimensional representation of constructs for use in various chronic diseases. Instruments that generalize across chronic diseases offer an opportunity to compare different conditions and study the possible common mechanisms that contribute to individual differences in health outcomes (see e.g., Felton & Revenson, 1984). In addition, the simultaneous assessment of both maladaptive and adaptive cognitions offers an opportunity to study the relatively unexplored role of adaptive mechanisms, for example, how and under what circumstances adaptive cognitions buffer the effects of maladaptive ones or show rather independent protective effects in adjustments to uncontrollable long-term conditions. Finally, research on the possible physiological, affective, and behavioral paths linking these cognitions to health and well-being in patients with chronic diseases could be encouraged.

Aside from research purposes, the psychometric properties of the ICQ are sufficiently high for clinical purposes. The comprehensive assessment of illness cognitions, applicable across diverse patient populations with chronic diseases, can serve as a complementary tool to medical diagnosis in screening for psychological risk factors in patients who may benefit from psychosocial interventions. Increasing knowledge about the mechanisms underlying their uniform effects can then stimulate the development of generic treatment components for various populations. Perhaps even more importantly, the identification of adaptive cognitions can lead to expanding these interventions by systematically building health-promoting processes (see e.g., Hayes et al., 1999). Particularly in the case of an inherently threatening circumstance, like a chronic disease, when the focus of attention is automatically directed to negative consequences, an incorporated stimulation of adaptive cognitions may considerably enhance the effectiveness of psychosocial treatments. With our present conceptualization and assessment of illness cognitions, we intended to take one further step in this direction, going beyond unfavorable thinking to what others have called a more strength-oriented, positive psychology in the face of uncontrollable long-term stress, such as a chronic disease (e.g., Gillham & Seligman, 1999).

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3

3.3 Physiological Pain Reactivity

Cognitive, behavioral and physiological reactivity to pain as predictor of long-term pain in rheumatoid arthritis patients

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ABSTRACT

A heightened reactivity to pain is assumed to play a significant role in the maintenance and exacerbation of pain in patients with chronic pain. In a prospective study involving 95 rheumatoid arthritis (RA) patients, the relative contribution of self-reported cognitive, behavioral and physiological components of pain reactivity were examined for a change in pain within 1 year. Regression analyses indicated that self-reported physiological reactivity predicted an increase in clinical and self-reported pain after 1 year, but not cognitive and behavioral reactivity. Neither disease activity nor neuroticism mediated or moderated the relationship of pain reactivity to long-term pain. However, structural equation modeling revealed that neuroticism directly affected physiological reactivity to pain, which in turn was the only significant predictor for subsequent pain. The results of this study underline the crucial role of physiological pain reactivity for exacerbation of pain in RA patients and are indicative for a symptom-specific pattern of physiological pain reactivity that is sustained by psychological predisposition and respondent learning processes.

INTRODUCTION

Pain is the most prominent physical complaint in rheumatoid arthritis (RA), a chronic inflammatory disease that primarily affects the joints. Although pain is a direct consequence of the disease process, patients' pain reports are usually only moderately related to the underlying pathology, and pain frequently becomes a problem in its own right. Variability in biomedical and psychosocial treatment outcomes, primarily geared to reducing the aversive consequences of pain instead of eliminating it, also indicate that pain remains one of the most complex factors in chronically painful disorders, such as RA.

In recent decades, biopsychosocial approaches have conceptualized pain as a multifaceted phenomenon that consists of at least three response systems, i.e. motor-behavioral, subjective-cognitive, and sensory-physiological components (Philips, 1977; Epstein et al., 1978; Lethem et al., 1983; Flor et al., 1990). In line with theories of emotion (e.g. Lang, 1968; Rachman & Hodgson, 1974; Borkovec et al., 1977), it is assumed that the degree of synchrony of these response systems varies: they are not necessarily commonly activated, might be maintained by different factors and might have differential effects on treatment outcomes. Studying their functional interrelationships and effects on long-term outcomes could provide a better understanding of the specificity of processes responsible for the maintenance and exacerbation of chronic pain.

In acute pain, pain responses involve the behavioral reaction of interrupting activity, cognitive attempts to direct attention to the aversive experiences to find a reasonable cause for the pain and prevent further damage, as well as physiological processes of heightened autonomic, somatosensory and central nervous system activity (see e.g. Flor et al., 1990). In as much as these responses are immediately triggered and functional for survival in instances of acute pain, they may be more loosely related and less protective in the event of chronic pain. In fact, maintenance of these reactions is thought to sustain and exacerbate pain and related outcomes, such as functional disability and depression. Based on predisposition and learning mechanisms, a habitual pattern of reactivity to pain, including avoidance behavior, cognitive preoccupation with bodily signals and heightened physiological arousal, might become increasingly chronic. This habitual pattern might be generalized to various stimuli associated with pain, function relatively independently of objective pathology and intensity of pain, and subsequently affect long-term pain outcomes (e.g. Lethem et al., 1983; Linton, 1985; Philips, 1987; Flor et al., 1990; Turk & Flor, 1999). Experimental and quasi-experimental studies have provided considerable evidence for the existence of these response patterns in chronic pain patients and for their maladaptive effects on pain outcomes, including pain itself.

Behavioral approaches predominantly focus on the prominent role of avoidance behavior in the maintenance and exacerbation of chronic pain through processes of external reinforcement or anticipatory anxiety (Fordyce, 1976; Lethem et al., 1983;

Linton, 1985; Philips, 1987). A considerable amount of research assessing avoidance behavior on the basis of observed or self-reported pain behavior (e.g. Philips & Jahanshahi, 1985b; Vlaeyen et al., 1990; Jensen et al., 1995) has demonstrated the major role of avoidance and its relationship to worse long-term outcomes in various chronic pain populations, including RA (Evers et al., 1998a; van Lankveld et al., 1998, 2000). Experimental studies have also supplied preliminary evidence for the maladaptive effects of avoidance on pain, demonstrating, for example, that avoidance of exposure can lead to decreased tolerance of stressful stimulation in migraine patients (Philips & Jahanshahi, 1985a).

Research on cognitive factors has emphasized the role of negative outcome expectancies with concepts such as catastrophizing or excessive worrying in the face of pain (see Keefe et al., 1989; Jensen et al., 1991b; Turk & Rudy, 1992; Aldrich et al., 2000). Results from pain coping and cognition measures that assess the extent that patients tend to catastrophize in the face of pain (e.g. Rosenstiel & Keefe, 1983; Sullivan et al., 1995; Kraaimaat et al., 1997) have provided considerable evidence for the prominent role of these cognitions in various chronic pain patients and their relationships to unfavorable pain outcomes (e.g. Keefe et al., 1989; Affleck et al., 1992; Martin et al., 1996). Moreover, experimental and longitudinal studies support the unfavorable effects of catastrophic thoughts on pain. For example, catastrophizing has been demonstrated to affect pain tolerance and pain intensity in experimentally induced pain (e.g. Spanos et al., 1979; Geisser et al., 1992; Sullivan et al., 1995). In prospective studies, catastrophizing or worrying in the face of pain predicted a worsening of various pain outcomes in RA patients (Keefe et al., 1989; Evers et al., 1998a), including pain itself (Keefe et al., 1989).

On the sensory-physiological level, reactivity to pain has been assumed to be particularly manifest in increased autonomic and muscular reactivity as well as the sensitization of central structures (Flor et al., 1990; Turk & Flor, 1999). Based on predisposition and/or respondent learning processes, these responses might develop in a chronic condition into a consistent, habitual pattern of reactivity to pain and pain-related stimuli that affect pain and related outcomes (see e.g. Flor et al., 1990; Turk & Flor, 1999). Evidence for stress- or pain-related patterns of heightened autonomic, somatosensory and/or central responses has been provided among various chronic pain patients, including those with RA (Salamy et al., 1983; Flor et al., 1985, 1992a, 1997; Jamner & Tursky, 1987; Lutzenburger et al., 1997; see also Anderson et al., 1985; Flor & Turk, 1989). Preliminary support also exists for the maladaptive function of physiological reactivity patterns on pain outcomes. For example, stress-induced increases in symptom-specific muscular tension predicted greater pain severity in depressed patients with chronic low back pain (Burns et al., 1997). In addition, self-reported autonomic arousal in the face of pain, assessed as

pain-related fears, predicted greater pain severity and more physical complaints in heterogeneous groups of chronic pain patients (McCracken et al., 1996, 1998).

In conclusion, there is empirical support for a multidimensional reactivity pattern to pain and its maladaptive effects in chronic pain patients. However, research usually focuses on just one component of response systems, such as pain behaviors, cognitive constructs or physiological responses (see Philips, 1987; Flor et al., 1990; McCracken et al., 1996). Other conceptualizations assess reactivity to pain as composite constructs without differentiating between response systems (see Jensen et al., 1991), such as pain-coping measures with confounding behavioral and cognitive responses (e.g. Brown & Nicassio, 1987). Both approaches preclude information about the possibly variable interrelationship between the response systems under different conditions and their relative contribution to pain outcomes. Integration and systematic comparison of these response systems could possibly clarify their common and independent response effects on chronic pain and provide a better understanding of the specificity of mechanisms underlying long-term pain.

Stress-vulnerability models suggest that the possible independent effects of the response systems might be the result of being differently determined by biomedical pathology and psychological vulnerability factors. It is usually assumed that pain reactivity is initiated and maintained by biomedical factors in an acute stage, but functions increasingly independently in a chronic stage (e.g. Lethem et al., 1983; Flor et al., 1985, 1990; Philips, 1987). However, since most of the research has been conducted with benign pain syndromes, where there is no biomedical indicator of pathology, the role of biomedical factors may be systematically underestimated. In pain syndromes with an underlying pathology of inflammatory activity, such as RA, where patients are recurrently confronted with unpredictable pain flare-ups, a habitual pattern of pain reactivity may be directly triggered and maintained by the disease process. In addition, pain reactivity has been demonstrated to be affected by psychological vulnerability factors, such as neuroticism or negative affectivity. Neuroticism and negative affectivity have been demonstrated to be related to avoidance behavior (Harkins et al., 1989; Wade et al., 1992), catastrophizing (Affleck et al., 1992; Martin et al., 1996) and physiological reactivity in chronic pain patients (Vlaeyen et al., 1999), suggesting a common underlying predisposition that possibly mediates or moderates the effect of pain reactivity on long-term pain (e.g. Affleck et al., 1992; Martin et al., 1996; Burns et al., 1997; Vlaeyen et al, 1999).

The purpose of the present study was to study the interrelationships of cognitive, behavioral and physiological response systems of pain reactivity in patients with RA and their concurrent relationships to disease severity and neuroticism. In addition, our object was to prospectively determine the role of these response systems for the long-term prediction of pain and study possible mediating or moderating effects of disease activity and neuroticism on this relationship. It was hypothesized (1) that the three response systems would

demonstrate closer relationships to neuroticism than to measures of disease severity, and (2) that initially higher levels of the response systems would predict an increase in pain within one year, after controlling for disease severity and neuroticism.

METHODS

Participants

The sample consisted of 95 outpatients with RA from two participating hospitals in the Netherlands. Inclusion criteria were a minimum age of 18 years and a diagnosis of RA according to American College of Rheumatology (ACR) criteria (Arnett et al., 1988). The sample was predominantly female (61%) and married (85%) with at least a primary or secondary level of education (28% and 63%, respectively). The mean age was 58.9 years (SD 11.6, range 33-82 years). The mean time since diagnosis was 15.9 years (SD 9.2, range 4-45 years).

Measures

Several clinical and self-report measures were assessed in the sample at two assessment points, with a mean time interval of one year.

Pain was assessed with a composite score of both clinical and self-report measures. Clinical pain ratings comprised the number of painful joints (Fuchs et al., 1989). Self-reports of pain were assessed with the Pain scale (6 items) of the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL; Huiskes, et al., 1990a; Evers et al., 1998b). The Pain scale is a disease specific scale for arthritis patients that assesses the severity and frequency of painful episodes and swollen joints and the duration of morning stiffness in the past month. Previous research showed reliability and validity of the IRGL to be highly satisfactory (Huiskes et al., 1990a; Evers et al., 1998b). Cronbach's alpha of the Pain scale in the present study was 0.86.

Disease activity was assessed with standardized erythrocyte sedimentation rate (ESR) laboratory measurements, which is an indicator of inflammatory activity in RA.

Cognitive and behavioral reactivity to pain were assessed with the Pain Coping Inventory (PCI; Kraaimaat et al., 1997; Evers et al., 1998a), a pain coping instrument which measures different cognitive and behavioral ways of dealing with pain on a 4-point Likert scale, ranging from 'rarely or never' (1) to 'very frequently' (4). Cognitive reactivity was assessed with the passive pain-coping scale Worrying (9 items), which measures negative pain cognitions. Representative items were: 'I start worrying when in pain' or 'I think that the pain will worsen'. Behavioral reactivity was assessed with a composite score of the passive pain

coping scales Resting and Retreating (12 items), measuring behavioral tendencies to restrict functioning and avoid environmental stimuli, respectively. Representative items of these scales were: 'I quit my activities', 'I rest by sitting or lying down' or 'If I am outdoors, I try to return home as soon as possible'. The reliability and validity of the PCI was supported by previous research on patients with RA, patients with chronic headache pain and patients attending pain clinics (Kraaimaat et al., 1997; Evers et al., 1998a). Cronbach's alpha in the present study was 0.74 for the cognitive and 0.77 for the behavioral reactivity to pain.

Physiological reactivity to pain was measured by various self-reported physiological reactions to pain, partly derived from the Physiological Anxiety Scale of the Pain Anxiety Symptoms Scale (PASS; McCracken et al., 1992). Respondents were asked to indicate how frequently they experience physiological reactions in the face of pain on a 4-point Likert scale, ranging from 'rarely or never' (1) to 'very frequently' (4). From a total pool of eight items, four items (i.e. trouble catching breath, heart racing, pressure in chest and panicking) had to be eliminated due to the infrequency of responses endorsed (skewness or kurtosis > 1.5). The items retained were: 'When in pain, I become dizzy or weak', 'I start sweating when in pain', 'I become restless when in pain' and 'When in pain, I have a tight or tense feeling in my body'. Internal scale consistency proved to be sufficient, as indicated by Cronbach's alpha of 0.71.

Neuroticism was measured by a Dutch version of the Eysenck Personality Questionnaire (EPQ; Wilde, 1970; Eysenck & Eysenck, 1991). Cronbach's alpha in the present sample was 0.85.

RESULTS

Patient Characteristics

Regardless of the long-term duration of arthritis in our sample (duration of disease was approximately 16 years), disease activity and pain levels were comparable to what have been previously reported in representative RA samples (Huiskes et al., 1990a; Evers et al., 1998b). On average, the moderate level of disease severity remained after one year, as indicated by nonsignificant changes in disease activity and pain. In addition, mean scores of the pain reactivity response systems were relatively stable and did not change within one year.

In terms of individual changes in the dependent variable, however, a review of the scatter plot indicated that there was considerable individual variation in pain, and 28% (n = 26) and 62% (n = 58) of the patients, respectively, showed a worsening or improvement in pain of 1 SD and 0.5 SD during the study period.

Correlates of Pain and Pain Reactivity

Pearson correlation coefficients between the cognitive, behavioral and physiological components of pain reactivity at first assessment indicated a moderate correlation between the different response systems (between 0.43 and 0.49; see Figure 1). In addition, all response systems demonstrated similar correlations with disease activity, pain and neuroticism (see Table 1). While correlations with disease activity were all nonsignificant, the response systems were weakly related or tended to be related to pain and all were moderately related to neuroticism, indicating more pain reactivity in patients with higher levels of pain and neuroticism. Finally, pain was also weakly related to higher levels of disease activity and neuroticism (for both $r = 0.28$, $p < 0.01$).

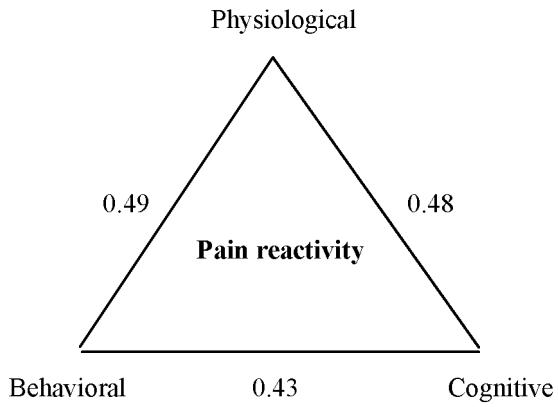

Figure 1 Interrelationships between response systems of pain reactivity. All correlations are significant at $p < 0.001$.

Predictors of Long-term Pain

Pearson correlation coefficients between the pain reactivity response systems at first assessment and residual gain scores of pain were calculated to explore the relationship between pain reactivity and long-term pain. Results indicated that one of the three response systems was significantly related to an increase in pain, i.e. physiological reactivity ($r = 0.40$, $p < 0.001$). In addition, behavioral reactivity tended to correlate with an increase in pain ($r = 0.20$, $p < 0.10$), while the correlation with cognitive reactivity was nonsignificant ($r = 0.07$, ns).

Table 1 Correlates of Response Systems of Pain Reactivity

	Behavioral	Cognitive	Physiological
Disease activity	0.07	0.02	0.16
Pain	0.18	0.23*	0.23*
Neuroticism	0.42***	0.49***	0.35**

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$.

Stepwise multiple regression analyses were then performed to examine the relative contribution of pain reactivity to the change in pain within one year, after controlling for possible confounding variables. Pain at second assessment was used as the dependent variable, controlling for the baseline scores of pain in the first step. The other control variables were entered in step 2, i.e. demographic variables (gender, age and educational level), disease activity and neuroticism, all measured at first assessment. In step 3, the different components of pain reactivity at first assessment were entered in the regression analyses. Results indicated that the best predictor for pain at second assessment was the initial level of pain, explaining 32% of the total variance. The control variables in step 2 did not add any variance. Pain reactivity in step 3, however, added 10% of the variance. Beta coefficients demonstrated that physiological reactivity significantly predicted an increase in pain after one year, but not cognitive and behavioral reactivity (see Table 2). When entering the different pain reactivity response systems separately in the regression analyses, again only physiological reactivity explained significant variance in long-term pain.

Table 2 Multiple Regression Analysis Predicting Long-term Pain

	β	Adj. ΔR^2
Pain T1 [a]	0.38***	0.32***
Control variables T1 [b]		0.00
Pain reactivity T1		0.10***
Behavioral	0.08	
Cognitive	0.10	
Physiological	0.33**	
Total adj. ΔR^2		0.42***

[a] T1: first assessment.
[b] Control variables: demographic variables (gender, age and educational level), neuroticism T1 and disease activity T1.
** $p < 0.01$ *** $p < 0.001$.

As visible from the results of Table 2, neither disease activity nor neuroticism mediated the effects of pain reactivity on long-term pain. To study possible moderator effects of disease activity and neuroticism, centered interaction terms with all pain reactivity components were entered in the regression analyses in step 4. Results again indicated that neither disease activity nor neuroticism moderated the relationship between pain reactivity and long-term pain.

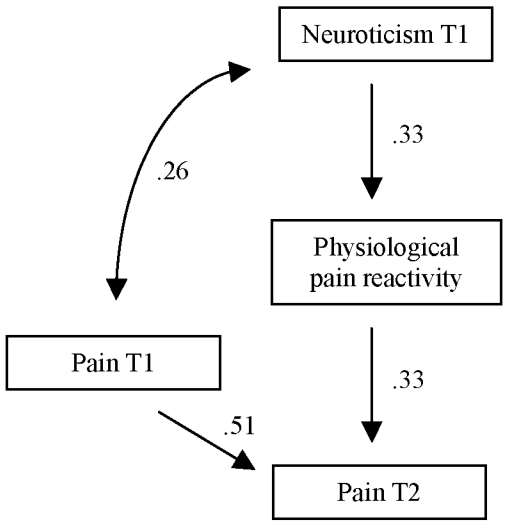

Figure 2 The significant paths (standardized regression coefficients) of the structural equation modeling, testing effects of pain reactivity at first assessment (T1) against pain at second assessment (T2), controlling for pain and neuroticism at first assessment (T1). Nonsignificant paths are omitted from the analyses. In addition, error variances are omitted from the figure for convenience of presentation. All paths are significant at $p < 0.01$.

The relative contribution of pain reactivity to subsequent pain was then tested in structural equation modeling, when taking the effects of disease activity and neuroticism into account (AMOS 4.0; Arbuckle, 1994). The same models were set up for all pain reactivity components in which the effects of pain reactivity at first assessment were tested against subsequent pain, controlling for pain, neuroticism and disease activity at first assessment. As in the regression analyses, only the

model for physiological reactivity provided a significant path to long-term pain. After omitting nonsignificant paths from this model (from disease activity to physiological pain reactivity, as well as from disease activity and neuroticism to subsequent pain), an excellent fit was revealed for the final model, in which neuroticism directly affected the physiological reactivity to pain. In turn, physiological reactivity was the only significant predictor of subsequent pain (χ^2 (2) = 1.89, p = 0.39; Goodness of Fit Index (GFI) = 0.99; Tucker Lewis Index (TLI) = 1.00; Incremental Goodness of Fit Index (IFI) = 1.00; see Figure 2).

DISCUSSION

A heightened reactivity to pain is assumed to contribute to the maintenance or exacerbation of pain in patients with chronic pain (e.g. Flor et al., 1990; Turk & Flor, 1999). However, little systematic research has been conducted on the different pain reactivity response systems (cognitive, behavioral and physiological) and their predictive value for pain in chronic pain patients. The focus of our study was to examine interrelationships of the pain reactivity response systems, their relationship to biomedical and psychological vulnerability factors and their effects on long-term pain in RA patients.

According to the assumed desynchrony of the response systems, the self-reported behavioral, cognitive and physiological components were moderately intercorrelated. This moderate degree of interdependence indicates that the response systems are not necessarily commonly activated and represent different dimensions of the pain experience, although they affect and probably enhance each other. In addition, all response systems demonstrated relatively uniform relationships to measures of disease severity and neuroticism. In accordance with what has previously been proposed on the basis of stress-vulnerability models (e.g. Flor et al., 1985, 1990), pain reactivity was hardly affected by disease severity, suggesting that it becomes a habitual response pattern in chronic pain and functions independently of actual pathology. In addition, the uniform relationship to neuroticism indicates a common underlying predisposition for vulnerability to stress. This psychological diathesis seems to be a relatively general pre-dispositional factor for heightened reactivity to pain, since correlations between neuroticism and avoidance behavior (Harkins et al., 1989; Wade et al., 1992), catastrophizing (Affleck et al., 1992; Martin et al., 1996) and physiological reactivity (Vlaeyen et al., 1999) have previously been reported in various chronic pain populations. Regardless of the similar relationships to these stress-vulnerability factors, response systems differently affected long-term pain. Results of multiple regression and structural equation modeling clearly indicated that the self-reported physiological reactivity to pain was the only significant predictor of

subsequent pain, independent of the effect of initial pain, disease activity, neuroticism and the other response systems. These results are in line with a previous cross-sectional study in which the self-reported physiological responses to pain predicted pain severity in a heterogeneous group of chronic pain patients, but not the behavioral or cognitive responses (McCracken et al., 1996). However, as far as we know, this is the first study that has compared response system effects on long-term outcomes and demonstrated maladaptive effects of self-reported physiological reactivity on chronic pain. Different physiological and/or cognitive-attentional mechanisms may account for these results.

Since the self-reported physiological reactivity was not related to disease activity and only very modestly to the intensity of present pain, it is unlikely that it represents symptomatic manifestations of the RA disease process. This lack of relationship to disease severity and the positive relationship to neuroticism instead suggest that it may be part of a psychophysiological response pattern. Peripheral physiological reactivity patterns in response to stressful and painful events as well as delayed return to baseline responses have previously been reported in various chronic pain patients (see Flor & Turk, 1989), including those with RA (e.g. Fisher & Cleveland, 1962; Moos & Engel, 1962; Walker & Sandman, 1977; Anderson et al., 1982), indicating heightened and/or prolonged muscular and autonomic reactivity when exposed to pain or stress.

The issue arises in so far as this self-reported physiological reactivity pattern reflects a symptom-specific physiological response in RA patients, as repeatedly reported in research on chronic benign pain (see Flor & Turk, 1989). Heightened EMG levels found only near painful joints support such a response specificity for RA patients as well (Moos & Engel, 1962; Walker & Sandman, 1977). In fact, the distribution of the self-reported physiological reactions initially assessed in our sample may indicate a symptom-specific pattern. Four items that primarily reflected respiratory and cardiovascular reactions had to be eliminated, due to the infrequency of endorsed responses. In contrast, this differentiation of the response pattern has not been reported in other chronic pain patients, where an adjusted version of the physiological reactivity scale (including respiratory and cardiovascular responses) has been used (McCracken et al., 1992, 1996, 1998; Larsen et al., 1997). To further explore the issue of response specificity, posthoc item analyses of the physiological reactivity scale were performed. Results indicated that all items demonstrated similar relationships to subsequent pain, suggesting a physiological response pattern consisting of both autonomic and somatosensory components that affect long-term pain. This pattern may be in agreement with the heightened and prolonged EMG and skin conductance levels that have been reported most consistently in RA patients when comparing physiological reactivity patterns to other chronic diseases (Fisher & Cleveland, 1962; Moos & Engel, 1962; Walker & Sandman, 1977; Anderson et al., 1982; see Anderson et al., 1985). Assuming a physiological basis for our self-report scale,

comparisons of psychophysiological response patterns between patients with RA and other chronic pain populations may clarify whether this reflects a RA-specific pattern or is part of a general reactivity pattern in chronic pain disorders.

Symptom-specific physiological patterns have frequently been found as reactions to pain-related or personally relevant stressors, suggesting that they may be enhanced by respondent learning processes (Flor et al., 1990; Turk & Flor, 1999). Respondent learning processes may also explain the great individual differences in self-reported physiological pain reactivity in our sample. Only 40% of the patients reported the physiological reactions to pain at least sometimes. In this subgroup, autonomic and somatosensory reactivity might have become a conditioned response to pain that maintains a pain-tension circle and exacerbates pain in the long run (Flor et al., 1990; Knost et al., 1999; Turk & Flor, 1999). However, it could also be argued on the basis of respondent learning processes that the self-reported physiological reactivity reflects general anxiety arousal, as suggested by research on pain-related fears (e.g. McCracken et al., 1992, 1996). Pain may then be enhanced due to anxiety-related autonomic and somatosensory activation in anticipation and as a consequence of pain (Flor et al., 1990; Turk & Flor, 1999). Although the physiological responses of both pain and anxiety have been demonstrated to be highly confounding and have considerable overlap (Gross & Collins, 1981), the kind of self-reported physiological reactivity in our sample, lacking cardiovascular and respiratory responses that are typical for the presence of general anxiety syndromes (Borkovec et al., 1977), do not solely support anxiety-related physiological reactions.

Admitting the limitation of self-report measures, the self-reported physiological reactions may also reflect a bias in attentional and interpretational processes, for example, a tendency to amplify pain-related responses, as suggested by research on hypochondria and hypervigilance (Pennebaker & Skelton, 1978; Chapman, 1986; Barsky et al., 1988; Rollman & Lautenbacher, 1993). Chronic pain patients have been shown to overemphasize physical symptoms (Flor et al., 1992b; Flor et al., 1999), and the high level of chronic pain patients' physical complaints in general and of those with high negative affectivity in particular have been frequently ascribed to attentional and interpretational biases (Harkins et al., 1989; Watson & Pennebaker, 1989; Affleck et al., 1992; Larsen, 1992; Wade et al., 1992; Smith et al., 1995). However, as pain-related fears, attentional and interpretational processes can not sufficiently explain the response specificity of the self-reported physiological pain reactivity, suggesting that these processes may only indirectly affect long-term pain by their relationship to patterns of physiological reactivity.

In contrast to physiological reactivity, behavioral and cognitive reactivity failed to affect long-term pain. It could be argued that the lack of effects for cognitive and behavioral reactivity might be due to the limited assessment of these responses systems with worry and avoidance behavior constructs. However, the selected constructs are theoretically grounded, and the present and similar assessments of

avoidance behavior and worry have previously been demonstrated as predictive of various long-term outcomes in arthritis patients (Keefe et al., 1989; Evers et al., 1998a; van Lankveld et al., 1999, 2000; Steultjens et al., 2001). Preliminary evidence also supports specific modality-related effects, depending on the type of response system: behavioral responses might most directly affect activity-related outcomes; cognitive responses, subjective-cognitive outcomes; and physiological responses, sensory-related outcomes. For example, avoidance behavior has most consistently been shown to predict functional disability and use of medication in prospective and treatment studies (e.g. Linton, 1986; Evers et al., 1998a; van Lankveld et al., 1999; Steultjens et al., 2001). Cognitive constructs of worrying or catastrophizing, although related to various long-term outcomes, including pain (Keefe et al., 1989), have been shown to affect the affective and evaluative components of pain, but not the sensory component (Geisser et al., 1994). In contrast to the study by Keefe et al. (1989), where a visual analogue scale (VAS) pain measure was used, our pain assessment consisted of both clinical and comprehensive self-report measurements that mainly reflected sensory aspects of pain (Fuchs et al., 1989; Evers et al., 1998b), suggesting - in agreement with previous cross-sectional research (McCracken et al., 1996) - that the sensory pain aspects are most directly affected by physiological reactivity patterns.

The results of our study, demonstrating effects for physiological pain reactivity on long-term RA pain, but not for the behavioral and cognitive reactivity, underscore the importance of assessing the response systems separately and studying their relative contribution to different pain outcomes. Increasing knowledge of the underlying mechanisms could eventually provide a better understanding of active treatment components and lead to more effective chronic pain modification procedures. For example, a response-specific pattern of physiological pain reactivity brings into question the sole application of anxiety-based treatments for reducing pain, since they might mainly affect the anxiety aspect of pain instead of the actual pain symptoms (Gross & Collins, 1981). A better understanding of the specificity of these mechanisms seems to be particularly useful for predicting long-term pain, since multidisciplinary treatments are currently primarily aimed at modifying secondary outcomes, such as depression and disability, instead of pain itself.

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4

Modification of Disease Outcome

Tailored Treatment in RA

Tailored cognitive-behavioral therapy in early rheumatoid arthritis for patients at risk: A randomized, controlled trial

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ABSTRACT

Recent developments in chronic pain research suggest that effectiveness of cognitive-behavioral therapy (CBT) may be optimized when applying early, customized treatments to patients at risk. For this purpose, a randomized, controlled trial with tailor-made treatment modules was conducted among patients with relatively early rheumatoid arthritis (RA disease duration of < 8 years), who had been screened for psychosocial risk profiles. All participants received standard medical care from a rheumatologist and rheumatology nurse consultant. Patients in the CBT condition additionally received an individual CBT treatment with two out of four possible treatment modules. Choice of treatment modules was determined on the basis of patient priorities, which resulted in most frequent application of the fatigue module, followed by the negative mood, social relationships and pain and functional disability modules. Analyses of completers and of intention-to-treat revealed beneficial effects of CBT on physical, psychological and social functioning. Specifically, fatigue and depression were significantly reduced at post-treatment and at the 6-month follow-up in the CBT condition in comparison to the control condition, while perceived support increased at follow-up assessment. In addition, helplessness decreased at post-treatment and follow-up assessment, active coping with stress increased at post-treatment, and compliance with medication increased at follow-up assessment in the CBT condition in comparison to the control condition. Results indicate the effectiveness of tailor-made CBT for patients at risk in relatively early RA, and supply preliminary support for the idea that customizing treatments to patient characteristics may be a way to optimize CBT effectiveness in patients with RA.

INTRODUCTION

In recent decades, the multiple disturbing effects of chronic pain on patients' physical, psychological and social functioning, such as increased functional disability and fatigue, heightened levels of anxiety and depression, and impaired social and economic functioning, has been widely recognized (e.g., Anderson et al., 1985; Chapman & Gavrin, 1999; Maniadakis & Gray, 2000; Gatchel, 2001). Medical treatment only partly alleviates these consequences of chronic pain, and psychosocial interventions - particularly cognitive-behavioral therapy (CBT) - have been shown to be a possibly effective adjunctive treatment for reducing the unfavorable effects on patient functioning (see e.g., McCracken, 1991; Hawley, 1995; Morley et al., 1999; van Tulder et al., 2000).

In spite of the encouraging effects of psychosocial interventions in chronic pain disorders, the variability in outcomes between patients and the magnitude and maintenance of effects in the long run is a point of continuing discussion (e.g., Turk, 1990; McCracken, 1991; DeVellis & Blalock, 1993; Keefe & van Horn, 1993; Hawley, 1995; Turk & Okifuji, 1998; Gatchel, 2001). Specifically, in patients with rheumatoid arthritis (RA), a chronic disabling disease that primarily affects the joints, meta-analyses have indicated that psychosocial interventions in general, and more specifically also CBT and behavioral treatments, have nonsignificant to small effects on indicators of physical and psychological functioning at post-treatment, and nonsignificant effects at follow-up assessments (Hawley, 1995, Riemsma et al., 2002; see also, McCracken, 1991; Riemsma et al., 1999). Meta-analyses of CBT for various chronic pain disorders, such as chronic low back pain or osteoarthritis, have revealed more promising effects, but improvement in magnitude and maintenance of effects is still desired (Hawley, 1995; Morley et al., 1999; van Tulder et al., 2000). The limited effects of CBT for RA and other chronic pain disorders have frequently been ascribed to the heterogeneity of patients. Not all patients may receive benefits from generic treatments. Instead, customizing treatments more closely to patient characteristics, in terms of patient selection and types and timing of treatment, has been repeatedly suggested as a way to optimize treatment effectiveness (e.g., Turk, 1990; McCracken, 1991; DeVellis & Blalock, 1993; Turk & Okifuji, 1998; van Tulder et al., 2000; Gatchel, 2001).

In view of the individual variability between patients with chronic pain, various attempts have been made to classify patients into more homogeneous subgroups and identify patients that may benefit from psychosocial interventions. For example, it has been repeatedly shown in various chronic pain disorders that subgroups of patients are relatively well-adjusted and might only receive limited benefits from CBT. Instead, it has frequently been suggested that the repeatedly identified group of patients with heightened distress levels and dysfunctional cognitive-behavioral factors benefit most from CBT (e.g., Turk & Rudy, 1988,

1990a; Turk, 1990; Main et al., 1992; Klapow et al., 1993, 1995; Strong et al., 1994; Turk & Okifuji, 1998; Gatchel, 2001). Retrospective analyses of CBT effects in fibromyalgia patients provided preliminary support for this view, indicating that patients characterized by high distress levels and dysfunctional cognitive-behavioral factors benefited more from CBT than those relatively well-adjusted or whose impairment was mainly related to social functioning (Turk et al., 1998). In RA, it is a well-known fact that subgroups of 20-40% of the patients suffer from heightened anxiety and depression levels (e.g., Frank et al., 1988; Murphy et al., 1988; Hawley & Wolfe, 1993; Evers et al., 1997, 2002a; Dickens et al., 2002). In addition, heightened distress levels in RA patients are directly related to cognitive-behavioral factors of illness cognitions, coping and social support, and these factors have in turn repeatedly been shown to prospectively predict the RA disease outcome. Specifically, there is evidence from prospective studies that illness cognitions of more helplessness and less acceptance, more passive coping with pain or stress, and lower levels of social support predict decreased physical, psychological and social functioning in RA patients in the long run (e.g., Brown & Nicassio, 1987; Brown et al., 1989a,b; Keefe et al., 1989; Smith & Wallston, 1992; Smith et al., 1994, 1997; Evers et al., 1997, 1998a, 2001a, 2002a; van Lankveld et al., 1999, 2000; Scharloo et al., 1999). In terms of patient selection, CBT treatment for RA patients is consequently likely to show increased magnitude and maintenance of effects for subgroups of patients with a psychosocial risk profile, including heightened distress levels and more dysfunctional cognitive-behavioral factors of illness cognitions, coping and social support.

In relation to treatment specificity, effect studies of CBT usually consist of generic treatments with multiple cognitive and behavioral modules, assuming that the different components are even relevant and effective for patients. However, in view of the various problems from which patients with chronic pain suffer, treatment programs applied modularly and tailored to patients' clinical needs may increase the effectiveness of CBT in chronic pain patients (e.g., Turk, 1990; Fry & Wong, 1991; Turk & Okofuji, 1998; Gatchel, 2001). The most frequently affected areas of pain, functional disability, fatigue, distress and impaired social functioning in RA patients are only moderately correlated (e.g., Huiskes et al., 1990a; Evers et al., 1997, 1998b; Huyser et al., 1998; see also McCracken, 1991), and these outcomes have been shown to be differently predicted by specific cognitive-behavioral factors in the long run (e.g., Smith et al., 1994, 1997; Evers et al., 1997, 1998a, 2001a,b, 2002a; Scharloo et al., 1999). Consequently, the effectiveness of CBT in RA may be optimized when interventions focus on specific outcomes of impaired functioning and the related cognitive-behavioral factors. In addition, applying treatment modules matched to individual patient profiles and directed to the outcome from which patients suffer most is likely to increase patient satisfaction with treatment and decrease attrition rates (see e.g., Turk & Rudy, 1990b).

It has also been assumed that treatment effectiveness depends on the timing of treatment, specifically the temporal stages of the illness. For example, it has been suggested that patients develop a relatively stable way of coping with chronic pain, and dysfunctional cognitive-behavioral factors may be less established and easier to modify at an earlier stage of the disease than later on, suggesting increased CBT effectiveness for patients suffering for a shorter time from their complaints (e.g., Philips & Jahanshahi, 1985b; DeVellis & Blalock, 1993; Peters et al., 2000; Sinclair & Wallston, 2001). In addition, interventions at an earlier stage of the disease have by definition a greater chance of having more long-term benefits and possibly preventing a worse long-term disease outcome, such as irreversible joint destruction in RA patients (Parker & Wright, 1995). Dysfunctional cognitive-behavioral factors' predicting a worse long-term disease outcome in RA patients has been shown to be already established in the initial years of the disease (Evers et al., 1997, 1998a, 2002a; Smith et al., 1997). In addition, retrospective analyses of previous CBT trials suggest improved effectiveness in patients with earlier RA, indicating more favorable changes in patients with a shorter duration of disease, particularly within the first 7 years (Kraaimaat et al., 1995a; Sinclair & Wallston, 2001). Moreover, a recently conducted CBT trial with early RA patients was the first controlled trial demonstrating beneficial effects on depression at post-treatment and follow-up assessment (Sharpe et al., 2001). Taken together, this provides preliminary evidence that CBT conducted at a relatively early stage of RA may improve effectiveness in the short and long terms.

Recent developments in multidisciplinary treatment for chronic pain increasingly include the regular care of nurse specialists, consisting of providing information and education about the medical treatment and counseling and advice on disease-related problems in daily life (e.g., Hill, 1997; Madigan & FitzGerald, 1999; Ryan, 2001; Temmink et al., 2001 for rheumatology). In rheumatology care, there is preliminary evidence supporting various beneficial effects of the care of a nurse specialist on indicators of physical and psychological functioning (Hill et al., 1994). In the Netherlands, regular consultations with a specialized rheumatology nurse - the rheumatology consultant - is a relatively common part of the standard medical care. If customized CBT for RA patients is an effective treatment for use in clinical practice, it is important to show adjunctive effects in addition to the standard care from the rheumatologist and the rheumatology consultant on physical, psychological and social functioning.

In the present study, the effects of tailor-made CBT for patients with relatively early RA who had been screened for a psychosocial risk profile was studied in addition to the standard medical care received from the rheumatologist and a rheumatology consultant. It was hypothesized that, in comparison to the control condition, patients in the CBT condition would demonstrate more favorable changes on indicators of physical, psychological and social functioning with at least small to medium effects at post-treatment and follow-up assessment.

METHODS

Patients and Procedure

Patients were randomly selected from patient medical records of three rheumatology outpatient clinics in the Netherlands. Inclusion criteria were a diagnosis of RA according to the American College of Rheumatology (ACR) criteria (Arnett et al., 1988), age above 18 years, and a duration of disease of less than 8 years. Patients with comorbid conditions that might interfere with the CBT treatment (such as malignancy, cardiac, respiratory, hepatic, and renal insufficiency) were excluded. In total, 407 patients who met inclusion criteria received a written invitation to take part in the questionnaire study. Of these patients, 278 (68%) agreed to participate. The participants were predominantly female (71%) and married or living with a partner (75%). The average age of patients was 55.24 (SD 12.20) with a 3.19 year mean duration of disease (SD 1.99). Fifteen percent of the patients had a primary level of education and 68% a secondary educational level (an average of 7 and 12 years of formal education, respectively).

Questionnaires were administered in this sample to screen for previously determined risk profiles. Risk profiles were based on the prevalence of heightened anxiety and negative mood levels in patients with early RA, as well as dysfunctional cognitive-behavioral factors of illness cognitions, coping and social support that have all been shown to prospectively predict the course of physical and psychological functioning in RA patients (Evers et al., 1997, 1998a, 2001a; Scharloo et al., 1999). Cutoff scores were based on findings from previous research, which showed that subgroups of approximately 30% of the patients suffer from subclinical levels of anxiety and depression (Evers et al., 1997, 2002a). The cutoff scores for cognitive-behavioral factors were accordingly established at 30% of previous RA patient norm groups (Evers et al., 1997, 1998a, 2001a, 2002a). Specifically, patients were classified at risk when scoring in the upper 30% in either anxiety or negative mood in comparison to norm groups of patients with early RA (Evers et al., 1997, 2002a), in conjunction with a score in the upper 30% of at least two out of the following six cognitive-behavioral factors: illness cognitions of heightened helplessness and low levels of acceptance (Evers et al., 2001a), a passive manner of coping with stress (Evers et al., 1997, 2002a), a passive manner of coping with pain (Evers et al., 1998a) and low levels of social functioning (size of social network and perceived support) (Evers et al., 1997, 1998a). In addition to the questionnaires' addressing the psychosocial risk profile, self-report measures of physical functioning (functional disability, pain and fatigue) were administered in this sample.

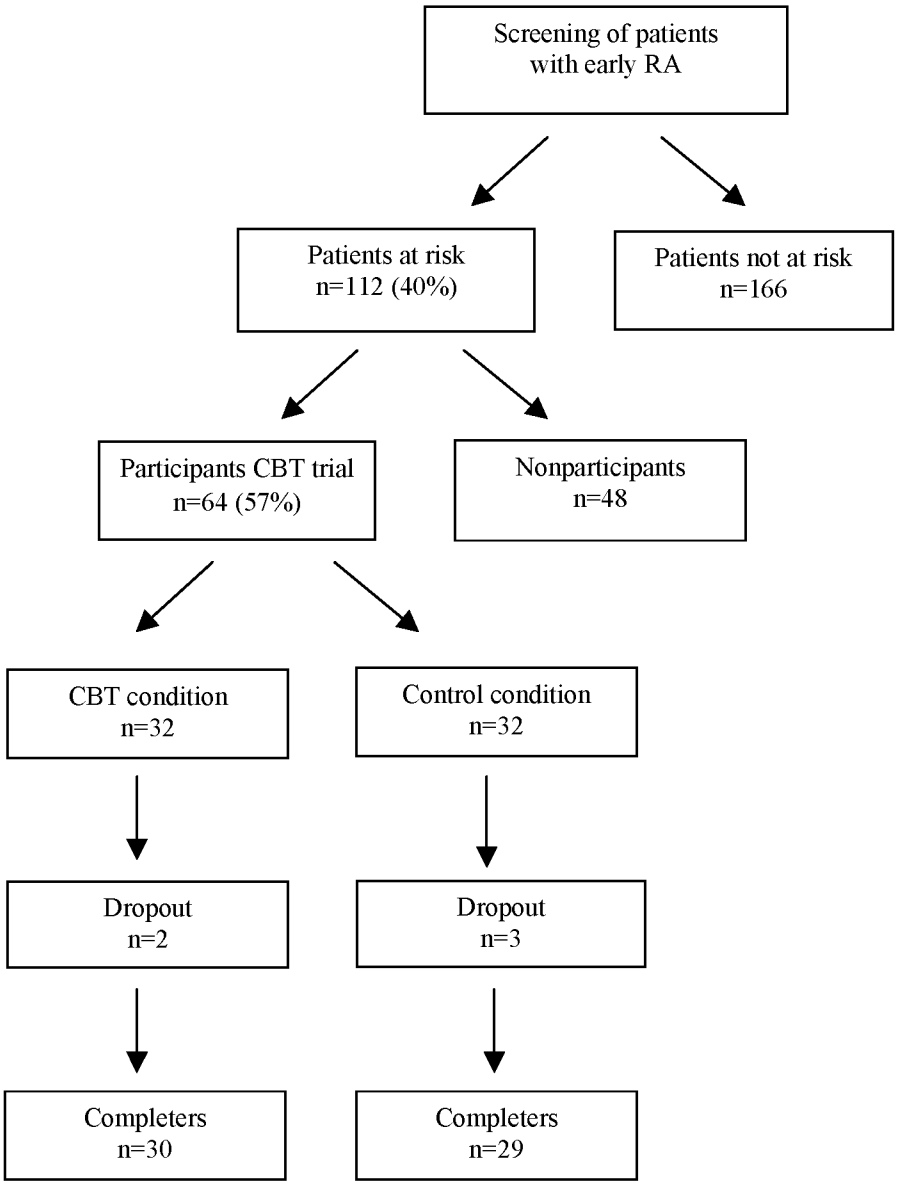

Figure 1 Overview of study participants

From the total sample of 278 patients, 112 patients (40%) met the criteria for a psychosocial risk profile (see Figure 1 for an overview of study participants). In accordance with the psychosocial risk profile criteria, patients at risk were characterized by significantly higher levels of negative mood and anxiety (t = 16.04, $p < 0.001$; t = 15.26, $p < 0.001$, respectively), as well as more dysfunctional cognitive-behavioral factors of greater helplessness and less acceptance (t = 9.81, $p < 0.001$; t = -7.65, $p < 0.001$, respectively), more passive coping with pain and stress (t = 7.24, $p < 0.001$; t = 2.51, $p < 0.05$, respectively), and lower levels of social functioning (t = -4.89, $p < 0.001$; t = -4.81, $p < 0.001$ for perceived support and the social network, respectively) in comparison to patients not at risk. In addition, patients at risk had a significantly lower educational level (t = -2.38, $p < 0.05$) and higher levels of functional disability, pain, and fatigue (t = 5.61; $p < 0.001$; t = 7.06, $p < 0.001$; t = 8.94, $p < 0.001$, respectively). No significant differences were found between the groups with regard to the demographic variables of gender, age, marital status or duration of disease.

Patients screened at risk received a written invitation within two weeks to take part in a randomized, controlled CBT trial for RA patients. From the 112 patients selected, 64 patients (57%) agreed to participate in the study. Reasons for refusing to participate related in most cases to practical concerns (63%), such as traveling distance and scheduling difficulties in combining the intervention with work and other daily activities. Twenty-five percent of the patients reported an unwillingness to participate due to a lack of interest, and 12% gave no reason for refusing. When comparing patients willing and unwilling to participate, there were no differences found between the groups in terms of demographic variables (gender, age, marital status, educational level), duration of disease, indicators of physical (functional disability, pain, fatigue) and psychological functioning (negative mood and anxiety), or any of the cognitive-behavioral factors (illness cognitions, coping with stress or pain, social functioning).

The 64 patients participating in the randomized trial were predominantly female (72%) and married or living with a partner (77%). Their average age was 54.13 (SD 11.17). Nine percent of the patients had a primary educational level and 75% a secondary educational level. Mean duration of disease was 3.45 years (SD 2.08) with the following distribution: 13 patients (20%) had a duration of disease of equal to or less than 12 months, 14 patients (22%) 13-24 months, 11 patients (17%) 25-36 months, 5 patients (8%) 37-48 months, 7 patients (11%) 49-60 months, 8 patients (13%) 61-72 months, 4 patients 73-84 months (6%) and 2 patients 85-90 months (3%). Most patients (72%) were taking a combination of disease modifying drugs (DMARD) and non-steroid anti-inflammatory drugs (NSAID). Twenty and 8%, respectively, exclusively used DMARD and NSAID. The 64 patients were randomly assigned to one of the two conditions (n = 32, for both conditions) according to a previously determined pattern of random numbers. Patients in both conditions received standard medical care from the rheumatologist

as well as quarterly consultations with the rheumatology consultant. Consultations with the rheumatology consultant consisted of providing information and education about the medical treatment and counseling and advice on disease-related problems in daily life. Patients in the CBT condition also received the tailor-made CBT treatment. Assessments of clinical data of disease activity (laboratory erythrocyte sedimentation rate (ESR) data and clinical joint score ratings) and self-report data took place at pretreatment (4-8 weeks after the screening assessment), at 6-month post-treatment and at a 6-month follow-up after post-treatment during routine medical visits by the rheumatology consultants. Joint score ratings were assessed by four rheumatology consultants who followed the patients over time, i.e. the same consultant scored patients at three times, at pretreatment, post-treatment and follow-up assessment. During these visits, patients also received the questionnaires which they were asked to complete at home. Before starting pretreatment assessment, the rheumatology consultants checked whether patients received any other psychological group or individual treatment. No patient was affected by this exclusion criterion at pretreatment or later.

Tailor-made CBT Treatment

Patients in the CBT condition received an additional cognitive-behavioral treatment within 6 months, consisting of in total 10 biweekly, 1-hour sessions and 1 final booster session scheduled four weeks later. The CBT condition consisted of individual treatment with 2 out of the 4 possible treatment modules that targeted the most frequently experienced problems with which RA patients have to cope: pain and functional disability, fatigue, negative mood and social relationships. Choice of treatment modules was determined on the basis of patient priorities. Information about the treatment and the different modules was given in the first session. In the following session, patients chose with the therapist assistance the treatment module they wanted to start with (first choice), as well as the module with which they wanted to continue (second choice). All treatment modules consisted of cognitive and behavioral interventions with homework assignments of about a half hour per day. The treatment modules were developed from standardized CBT protocols of RA patients (e.g., Kraaimaat et al., 1995a), as well as standardized CBT protocols of pain, fatigue, mood disorders and social functioning problems (e.g., Barlow, 1993; Hawton et al., 1989; Gatchel & Turk, 1996). The pain and function disability module consisted of progressive relaxation, attention diversion, stimulation of physical exercising in daily life in the face of the current physical condition, activity pacing, problem-solving, adjustment of goal-setting to the current physical condition, identification of pain-provoking cues in daily life, and cognitive restructuring of dysfunctional pain cognitions. The fatigue module included activity-pacing, adjustment of goal-setting to the current physical condition, setting priorities and structured planning of daily activities and time off, and cognitive restructuring of activity demands. The negative mood module

consisted of problem-solving, cognitive restructuring of depressogenic and anxious cognitions, identification of stress-provoking cues in daily life, stimulating pleasurable activities and restructuring of goal-setting in the face of the current physical condition, emotional processing of the changes RA has brought about in daily life and finding benefits. The social module finally included identification of social stress provoking cues in daily life, cognitive restructuring of social anxious cognitions, stimulating social activities in the face of the current physical condition, and social skills training including help-seeking behavior and communication about RA. In all treatment modules, the final booster session dealt with relapse prevention and further improvement of the attained goals. Patients were treated by two therapists trained in the treatment modules and supervised by a cognitive-behavior supervisor. Sessions were tape recorded and reviewed by the supervising cognitive-behavioral therapist for the accuracy of applying the treatment modules. In addition, an independent cognitive-behavioral therapist uninvolved in the present study reviewed 10% of randomly selected tapes and confirmed the therapists' adherence to the treatment modules.

Measures

Demographic variables were assessed with a general checklist, assessing patients' gender, age and marital status. In addition, educational level was measured using 7 categories that can be classified as primary, secondary and tertiary educational levels, representing on average 7, 12, and 17 years of education, respectively.

Disease activity was assessed in patients participating in the randomized trial with the Disease Activity Score (DAS; Prevoo et al., 1995), which consists of a weighted composite score of ESR (1-140mm first hour) and clinical joint score ratings (number of painful and swollen joints; Fuchs et al., 1989).

Functional disability was assessed with a composite score of the Mobility and Self-care scales of the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL; Huiskes et al., 1990a; Evers et al., 1998b), a questionnaire derived from the Arthritis Impact Measurement Scales (AIMS; Meenan et al., 1980), which assesses physical, psychological and social health in patients with rheumatic diseases. Previous research has shown that the reliability and validity of the IRGL scales are highly satisfactory (Huiskes et al., 1990a; Evers et al., 1998b). The Mobility and Self-care scales, which assess the functional capacities of the lower and upper extremities, respectively, over the last month (15 items) have been shown to be highly comparable to the AIMS physical functioning scales (Evers et al., 1998b). A composite score of the scales was calculated by adding the standardized scores (*z*-scores) of both indicators. A higher composite score indicates higher levels of functional disability.

Pain was assessed with the IRGL Pain scale (6 items), measuring the severity and frequency of painful episodes and swollen joints and duration of early morning stiffness in the last month.

Fatigue was assessed with the Fatigue scale (8 items) of the Checklist Individual Strength (CIS; Vercoulen et al., 1996), measuring patients' level of fatigue for the previous two weeks.

Psychological functioning was measured by the IRGL Anxiety and Negative Mood scales. The Anxiety scale is a shortened version of the Dutch State Anxiety Scale (10 items) (Spielberger, 1970; van der Ploeg et al., 1980), assessing anxiety levels in the last month. The Negative Mood scale (6 items) is derived from Zwart and Spooren's questionnaire (Zwart & Sporen, 1982) and assesses various negative mood states over the previous two weeks. In addition, depression was assessed with a Dutch version of the Beck Depression Inventory (BDI; Beck et al., 1988) in the patients participating in the randomized trial.

Social functioning in the past six months was measured with the IRGL social functioning scales, reflecting a quantitative and qualitative aspect of social support. The qualitative aspect was measured with the Perceived Support scale (5 items), inquiring about perceived availability of emotional and instrumental support (availability to share sad and pleasant events, get support when faced with stress and pain, get help for casual work). The quantitative aspect was assessed by the size of the social network, i.e. the number of friends and family members with whom patients associate.

Illness cognitions were measured with the Illness Cognition Questionnaire (ICQ; Evers et al., 2001b), assessing different ways of cognitive adjustment to a chronic disease. Two scales were used in the present study: helplessness (focusing on the adverse aspects of the disease and generalizing them to daily functioning, 6 items) and acceptance (recognizing the need to adapt to a chronic disease while perceiving the ability to tolerate and manage its aversive consequences, 6 items).

Coping with stress was assessed with the Utrecht Coping List (UCL; Schreurs et al., 1993), a well-documented coping questionnaire in the Netherlands (see e.g., Evers et al., 1997, 2001a, 2002a; Scharloo et al., 1999, for use in RA patients), adopted from Westbrook (1979), which measures active and passive coping strategies when dealing with everyday problems. Active coping was assessed with the Problem focusing scale (7 items), measuring cognitive and behavioral efforts to apply goal-oriented problem-solving strategies. Passive coping was measured with the Avoidance scale (8 items), measuring cognitive and behavioral attempts to avoid, escape from and acquiesce when facing everyday problems.

Coping with pain was assessed by the Pain Coping Inventory (PCI; Kraaimaat et al., 1997; Evers et al., 1998a) measuring active and passive coping strategies when dealing with pain. Active pain coping strategies reflect three cognitive-behavioral strategies, measuring patients' efforts to distract themselves from the pain (Distraction, 5 items), to reinterpret and transform the pain (Pain

Transformation, 4 items) and to function in spite of the pain (Reducing Demands, 3 items). Passive pain coping reflects three cognitive-behavioral strategies, assessing behavioral tendencies to restrict functioning (Resting, 5 items), to avoid environmental stimuli (Retreating, 7 items) and catastrophic cognitions about the pain (Worrying, 9 items). A composite score of active and passive pain coping can be calculated by summing up the nonweighted scores of the three active and passive coping strategies (Kraaimaat et al., 1997; Evers et al., 1998a).

Compliance with RA medication was assessed on a 3-point scale by a single item, inquiring about the frequency of failing to take the prescribed RA medication during the previous month (1 = once a week or more, 2 = less than once in a week, 3 = never).

Statistical Analyses

Due to slight skewed distributions of scores at negative mood (skewness or kurtosis above 1.5), square root transformation was applied. Social network scores were categorized according to norm classes (Huiskes et al., 1990a). Differences between subgroups at the time of screening (patients at risk versus not at risk, participants in the CBT trial versus refusers) and at pretreatment (CBT condition versus control condition, dropouts versus completers) were tested with chi-square analyses for categorical variables and Student's *t*-test for continuous variables with a threshold of $p < 0.05$ (two-tailed). In the event of significant differences or tendencies of differences ($p < 0.10$) between the CBT and control conditions, these variables were taken into account as covariates in the repeated measurement analyses. According to the treatment modules, treatment effects were expected in the primary outcome measures of physical (functional disability, pain, fatigue), psychological (depression, negative mood and anxiety) and social functioning (perceived support, size of the social network). Disease activity and cognitive-behavioral factors of illness cognitions, coping with stress and pain, and compliance were regarded as secondary outcome measures. A general linear model for repeated measurement was used to analyze the effects of CBT on the primary and secondary outcome variables, with time (three levels) as fixed factor. Multivariate analyses were conducted for the primary outcomes of physical, psychological and social functioning, and univariate analyses for the secondary outcomes. In the case of significant group x time interactions, paired *t*-tests between pretreatment and post-treatment and between pretreatment and follow-up assessment were conducted separately for both conditions to gain a better understanding of the nature of the interaction. Effect sizes were calculated by the difference between the means of the assessment points divided by their pooled standard deviations. All analyses were conducted with completers as well as with intention-to-treat analyses, using the last-observation-carried-forward method. Since both methods revealed the same results overall, only analyses with completers will be presented.

RESULTS

Pretreatment Condition Comparisons

Means and SDs of demographic variables, duration of disease, use of medication, disease activity, indicators of physical, psychological and social functioning and cognitive-behavioral factors are presented for both conditions separately in Tables 1, 3 and 4. Pretreatment comparisons of both conditions revealed no significant differences between the groups in relation to demographic variables (gender, age, marital status, educational status), duration of disease, use of medication, disease activity, the indicators of physical, psychological and social functioning or any of the cognitive-behavioral factors. However, a tendency was found for the level of education. Patients in the CBT condition tended to have a higher educational level than patients in the control condition ($t = 1.85$, $p = 007$). Consequently, educational level was used as a covariate in all repeated measurement analyses. Finally, patients in the conditions did not differ on medication at post-treatment and follow-up assessment.

Table 1 Means (and SDs) or Percentages of Demographic Variables, Duration of Disease and Medication in the CBT Condition (CBT: $n = 30$) and the Control Condition (CC: $n = 29$) at Pretreatment

	CBT	CC
Gender	70%	72%
Married	83%	72%
Age (years)	53.9 (10.3)	53.5 (12.6)
Duration of disease (years)	2.7 (1.9)	3.5 (2.1)
Educational level		
Primary	6%	10%
Secondary	67%	87%
Tertiary	27%	3%
Medication		
NSAID	73%	83%
DMARD	90%	97%

Dropouts

Between pretreatment and follow-up assessment, 5 patients (8%) dropped out: 3 patients from the control condition and 2 patients from the CBT condition. Reasons for dropping out were the occurrence of stressful life events for one patient from both conditions (divorce and a partner's serious medical condition),

lack of sustained motivation to participate in the study for two patients in the control condition, and incomplete questionnaire assessment for one patient in the treatment condition. When comparing the dropouts to the completers at pretreatment, no significant differences were found between the groups regarding demographic variables (gender, age, marital status, educational level), use of medication, duration of disease, or the indicators of physical, psychological and social functioning.

Treatment Modules in the CBT condition

The frequency of treatment modules applied, representing patients' first and second choices, are presented in Table 2, indicating preference differences in treatment modules: the fatigue and negative mood modules were applied to about two third of the patients as first or second choice (63% and 57%, respectively), while the social relationship and pain and functional disability modules were applied to less than half of the patients (43% and 37%, respectively).

Table 2 Frequency of Treatment Modules Applied in the CBT Condition (n = 30)

	Pain/Functional disability	Fatigue	Negative mood	Social relationships
First choice	5	15	10	0
Second choice	6	4	7	13
Not applied	19	11	13	17

Outcome in Disease Activity

The general linear model for repeated measurement regarding disease activity revealed a time effect for both conditions ($F(2,55) = 3.77$, $p < 0.05$), indicating that disease activity decreased during the study period for both conditions (see Table 3). No significant time x condition effect was found for disease activity ($F(2,55) = 2.03$, $p < 0.14$).

Outcome in Physical, Psychological and Social Functioning

The general linear models for repeated measurement did not reveal any significant time effects for the conditions for the indicators of physical, psychological and social functioning (see Table 3).

Table 3 Means (and SDs) of Disease Activity, Physical, Psychological and Social Functioning in the CBT Condition (CBT: n = 30) and the Control Condition (CC: n = 29) at Pretreatment, Post-treatment and the Follow-up Assessment

		Pretreatment	Post-treatment	Follow-up assessmemt
Disease activity				
	CBT	3.23 (1.45)	2.93 (1.49)	2.92 (1.57)
	CC	3.00 (1.15)	2.85 (1.13)	2.46 (0.88)
Physical functioning				
Funct. disability	CBT	2.41 (0.43)	2.46 (0.47)	2.42 (0.47)
	CC	2.44 (0.36)	2.40 (0.38)	2.37 (0.40)
Pain	CBT	15.40 (3.86)	14.93 (5.32)	14.99 (5.12)
	CC	16.28 (4.83)	15.35 (4.55)	15.79 (4.98)
Fatigue	CBT	40.07 (8.90)	34.70 (10.56)	35.18 (11.51)
	CC	39.38 (9.86)	37.41 (11.35)	41.38 (11.84)
Psychological functioning				
Depression	CBT	12.79 (6.49)	9.98 (4.62)	9.51 (5.35)
	CC	12.18 (6.70)	12.85 (7.87)	13.07 (7.51)
Negative mood	CBT	2.20 (0.86)	1.77 (1.08)	1.81 (0.95)
	CC	2.42 (0.98)	2.33 (1.04)	2.43 (0.98)
Anxiety	CBT	22.23 (5.26)	19.37 (4.72)	20.66 (5.81)
	CC	24.04 (5.56)	22.52 (6.30)	22.55 (5.45)
Social functioning				
Perceived support	CBT	13.30 (4.02)	13.90 (3.49)	14.74 (3.53)
	CC	14.07 (3.75)	13.93 (3.78)	13.45 (3.87)
Social network	CBT	1.87 (0.94)	1.93 (0.74)	1.78 (0.48)
	CC	1.61 (0.56)	1.79 (0.62)	1.86 (0.92)

When comparing both conditions, multivariate analyses of the indicators of physical functioning (functional disability, pain, fatigue) revealed a significant time x condition effect, Wilks' $\lambda = 0.73$, $F(6,51) = 3.16$, $p < 0.05$. Univariate tests indicated a significant time x condition effect for fatigue ($F(2,55) = 4.17$, $p < 0.05$). Paired t-tests showed that fatigue significantly decreased in the CBT condition at post-treatment and follow-up assessment ($t = 3.09$, $p < 0.01$ and $t = 3.14$, $p < 0.01$, respectively), but not in the control condition ($t = 1.18$, $p = 0.25$ and $t = -1.44$, $p = 0.16$, respectively). Univariate condition x time interactions were not significant for functional disability and pain ($F(2,55) = 1.82$, $p = 0.17$ and $F(2,55) = 0.27$, $p = 0.77$, respectively).

Table 4 Means (and SDs) of the Cognitive-Behavioral Factors in the CBT condition (CBT: n = 30) and the Control Condition (CC: n = 29) at Pretreatment, Post-treatment and the Follow-up Assessment

		Pretreatment	Post-treatment	Follow-up assessmemt
Illness cognition				
Helplessness	CBT	12.93 (3.61)	11.33 (3.75)	11.79 (3.45)
	CC	12.93 (3.41)	13.04 (3.82)	12.66 (3.41)
Acceptance	CBT	14.13 (4.60)	15.70 (4.12)	16.26 (3.97)
	CC	13.45 (3.63)	14.21 (3.82)	14.28 (3.55)
Coping with stress				
Active	CBT	2.48 (0.51)	2.67 (0.55)	2.60 (0.48)
	CC	2.29 (0.41)	2.23 (0.45)	2.27 (0.44)
Passive	CBT	2.00 (0.56)	1.95 (0.49)	1.96 (0.40)
	CC	2.19 (0.38)	2.18 (0.33)	2.17 (0.36)
Coping with pain				
Active	CBT	2.35 (0.39)	2.27 (0.27)	2.19 (0.37)
	CC	2.31 (0.41)	2.13 (0.40)	2.22 (0.38)
Passive	CBT	2.08 (0.43)	2.04 (0.33)	1.98 (0.34)
	CC	2.01 (0.41)	1.98 (0.45)	1.95 (0.42)
Compliance				
	CBT	2.67 (0.66)	2.73 (0.52)	2.85 (0.35)
	CC	2.79 (0.49)	2.52 (0.78)	2.59 (0.78)

With regard to psychological functioning, a significant condition x time interaction was found in the multivariate analyses for the indicators of psychological functioning (depression, negative mood, anxiety), Wilks' $\lambda = 0.73$, $F(6,51) = 3.20$, $p < 0.05$. Univariate tests showed a significant time x group interaction effect for depression ($F(2,55) = 5.34$, $p < 0.01$), demonstrating that depression significantly decreased in the CBT condition at post-treatment and follow-up assessment ($t = 3.02$, $p < 0.01$ and $t = 3.10$, $p < 0.01$, respectively), but not in the control condition ($t = -0.57$, $p = 0.58$ and $t = -1.23$, $p = 0.23$, respectively). No significant effects of condition x time interactions were revealed for negative mood and anxiety ($F(2,55) = 1.30$, $p = 0.28$ and $F(2,55) = 0.67$, $p = 0.52$, respectively). However, due to the significant effects on depression, the course of negative mood and anxiety were additionally explored for both conditions, indicating that negative mood significantly decreased in the CBT

condition at post-treatment and follow-up assessment (t = 2.25, p < 0.05 and t = 2.02, p = 0.05, respectively), but not in the control condition (t = 0.43, p = 0.67 and t = -0.07, p = 0.94, respectively). In addition, anxiety significantly decreased in the CBT condition at post-treatment (t = 3.46, p < 0.01), but not at the follow-up assessment (t = 1.63, p = 0.11). However, anxiety also tended to decrease in the control condition at both assessment points (t = 1.68, p = 0.10 and t = 1.97, p = 0.06, respectively).

For indicators of social functioning, a nearly significant condition x time interaction was found in the multivariate analyses of social functioning (perceived support, size of the social network), Wilks' λ = 0.84, F(4,53) = 2.55, p = 0.05. Univariate analyses revealed a significant time x group interaction for perceived support (F(2,55) = 4.17, p < 0.05), showing that perceived support significantly increased in the CBT condition at follow-up assessment (t = -3.18, p < 0.01), but not at post-treatment (t = -1.28, p = 0.21). Perceived support did not significantly change in the control condition (t = 0.27, p = 0.79 and t = 1.57, p = 0.13, respectively). No significant time x condition effect was found for the size of the social network (F(2,55) = 1.45, p = 0.24).

Outcome in Cognitive-Behavioral Factors

The general linear models for repeated measurement of the cognitive-behavioral factors of illness cognition, coping with stress or pain, and compliance did not indicate a significant time effect for both conditions (see Table 4). When comparing both conditions, a significant condition x time interaction was found for active coping with stress (F(2,55) = 3.85, p < 0.05). Paired t-tests revealed that patients in the CBT condition used significantly more active coping strategies when dealing with stress at post-treatment (t = -2.88, p < 0.01), but not at follow-up assessment (t = -1.44, p = 0.16), while active coping with stress did not significantly change in the control condition at both assessment points (t = 0.80, p = 0.43 and t = 0.22, p = 0.83, respectively). Moreover, tendencies for condition x time interactions were found for cognitions of helplessness (F(2,55) = 2.47, p = 0.09) and compliance with RA medication (F(2,55) = 2.51, p = 0.09). Paired t-tests demonstrated that helplessness significantly decreased in the CBT condition at post-treatment and follow-up assessment (t = 2.98, p < 0.01 and t = 2.37, p < 0.05, respectively), but not in the control condition (t = -0.22, p = 0.83; t = 0.62, p = 0.54). In addition, compliance with RA medication significantly increased in the CBT condition at follow-up assessment (t = -2.08, p < .05), but not at post-treatment (t = -0.57, p = 0.57), while compliance tended to decrease in the control condition at post-treatment and follow-up assessment (t = 1.98, p = 0.06; t = 1.80, p = 0.08, respectively). No significant time x interaction effects were revealed for illness cognitions of acceptance, active and passive coping with pain or passive coping with stress (F(2,55) = 1.13, p = 0.33; F(2,55) = 2.15, p = 0.13; F(2,55) = 0.17, p = 0.85; F(2,55) = 0.31, p = 0.74, respectively).

Effect Sizes

Effect sizes of the primary outcome measures with significant effects indicated overall medium effects for the CBT condition at post-treatment and follow-up assessment (Cohen, 1988): effect sizes were 0.55 and 0.48 for fatigue and 0.51 and 0.55 for depression at post-treatment and follow-up assessment, respectively. In addition, small to medium effects were found for negative mood, anxiety and perceived support at post-treatment and follow-up assessment (0.44 and 0.43 for negative mood, 0.57 and 0.28 for anxiety, and 0.16 and 0.38 for perceived support at post-treatment and follow-up assessment, respectively). In contrast, effect sizes on these primary outcomes in the control condition were all negative, except for fatigue and negative mood at post-treatment (0.19 and 0.01, respectively) and anxiety at post-treatment and follow-up assessment (0.26 and 0.27, respectively).

DISCUSSION

This trial of customized CBT for patients with relatively early RA indicated that, in addition to the standard care provided by a rheumatologist and a rheumatology consultant, tailor-made treatment offered to individual patients at risk has beneficial effects on primary outcomes of physical, psychological and social functioning, and these effects were generally maintained at follow-up assessment. Specifically, favorable effects on primary outcomes were found for fatigue and depression at post-treatment and follow-up assessment, as well as for perceived support at follow-up assessment. Exploration of secondary outcomes of cognitive-behavioral factors supported additional beneficial effects, including increased active coping with stress at post-treatment, decreased helplessness at post-treatment and follow-up assessment, as well as increased compliance at follow-up assessment in the CBT condition in comparison to the control condition, generally suggesting that offering tailored CBT to RA patients at risk may be a promising way to optimize treatment effectiveness.

Participants in the CBT trial consisted of patients with relatively early RA who had been screened for a psychosocial risk profile. The screening sample was comparable to representative samples of patients with early RA with regard to demographic variables, levels of physical, psychological and social functioning and cognitive-behavioral factors (Meenan et al., 1991; Evers et al., 1997, 1998a, 2002a). In accordance with the empirically derived screening criteria (Evers et al., 1997, 1998a, 2001a, 2002a; Scharloo et al., 1999), patients at risk were characterized by lower levels of physical, psychological and social functioning and more dysfunctional cognitive-behavioral factors, in comparison to patients not at risk. For patients participating in the CBT trial, results suggest that there was no systematic bias in the selection of patients. Reasons for refusing to take part in the CBT trial were in most cases related to practical concerns, and participants did not

differ from nonparticipants with regard to demographic variables, levels of physical, psychological and social functioning or cognitive-behavioral factors. Finally, dropout rates were generally low for the CBT and the control conditions (6% and 10%, respectively), and statistical analyses of completers and intention-to-treat analyses revealed the same results overall.

Effects found on the primary outcomes of fatigue, depression and perceived support corresponded to the three treatment modules most frequently applied in the CBT condition. Application of treatment modules was based on patients' priorities, which were highest for the fatigue module, followed by the negative mood, social relationships and pain and functional disability modules. In particular, fatigue has only recently received attention as a frequent problem for RA patients and as a possible focus for psychosocial interventions (Belza, 1995; Huyser et al., 1998; Barlow et al., 2000). In accordance with a nearly significant effect found for fatigue in a recently conducted self-management trial (Barlow et al., 2000), our results indicate that fatigue can be significantly reduced by CBT. In addition, psychological functioning was improved by decreased depression and, as in the case of fatigue, these effects were stable at follow-up. Previous CBT trials with RA patients only incidentally reported beneficial effects on depression or other outcomes of psychological functioning (cf., Bradley et al., 1987; O'Leary et al., 1988; Sharpe et al., 2001). As for social functioning, there is only one study that previously reported beneficial effects of CBT on an indicator of social support at post-treatment (O'Leary et al., 1988), while perceived support in our study increased in the treatment condition at follow-up assessment.

Effect sizes found for these primary outcomes supply preliminary support for the idea that tailor-made treatment for patients with relatively early RA can improve treatment effectiveness. Effect sizes for the primary outcome measures indicated overall medium effects for fatigue and depression at post-treatment and follow-up assessment, as well as small to medium effects for perceived support at follow-up assessment (Cohen, 1988). In contrast, a recently conducted meta-analysis of controlled trials of psychosocial interventions for patients with RA revealed nonsignificant to small effects for physical and psychological functioning at post-treatment, and nonsignificant effects at follow-up assessment (Riemsma et al., 2002; see also Hawley, 1995; Riemsma et al., 1999). When exclusively CBT trials or behavioral treatments for RA patients are considered (Hawley, 1995; Riemsma et al., 2002), results are about the same. Although comparisons to other trials must be cautiously interpreted due to differences between studies in type of intervention, control groups, designs, outcome measures and settings, these findings generally suggest that increased effect sizes at post-treatment and follow-up assessment may be an adjunctive value of tailor-made CBT in relatively early RA.

Treatment effectiveness could also be optimized when interventions change dysfunctional cognitive-behavioral factors at an early stage of the disease and

possibly prevent a worse long-term disease outcome. Our results indicated beneficial changes at follow-up assessment in disease-related cognitive-behavioral factors, such as reduced helplessness in handling RA and its consequences and increased compliance with RA medication. In addition to previous findings of beneficial effects of CBT on helplessness in longstanding RA (Parker et al., 1995), our results indicate that helplessness can be modified at a relatively early stage of the disease, and effects were maintained at follow-up assessment. Taking into account that the findings for compliance should be regarded as explorative due to the single-item assessment, the effects on compliance may be particularly likely to provide a long-term benefit by reducing the risk of an unfavorable disease process (Radojevic et al., 1992) and decreasing the costs of medical treatment (Lorig et al., 1993).

The beneficial effects of CBT were found as an addition to the standard medical care received from a rheumatologist and a rheumatology consultant. In view of the preliminary findings of beneficial effects of the rheumatology consultant on indicators of physical and psychological functioning (see, Hill et al., 1994) and the fact that consultations with the rheumatology consultant have a variety of aspects in common with CBT, such as providing support and empathy, problem-solving related to the limitations of daily activities (e.g., returning to work, helping in housekeeping, adjustment of home facilities), as well as stimulation of favorable health behaviors (e.g., compliance, activity pacing and exercising), the present trial gives a rather conservative estimate of the contribution of tailored CBT.

A low rate of attrition has been suggested as another proxy outcome variable of treatment effectiveness (Turk & Rudy, 1990b). In contrast with dropout rates of about 45% found in a meta-analysis of psychosocial interventions (see Wierzbicki & Pekarik, 1993), the relatively low 6% dropout rate in the treatment condition indicated high treatment acceptance, possibly due to the use of customized treatment modules applied on the basis of patient priorities. In addition, patients with a psychosocial risk profile are likely to be motivated for CBT and pretreatment screening of patients at risk may have a favorable effect on attrition rates.

Despite its relatively promising results, the present study had several limitations. Most importantly, we did not directly test the hypothesis that tailored CBT for patients at risk at an early stage of the disease may be superior to general CBT treatments for all RA patients, and consequently information is unavailable about the specific treatment characteristics to which the beneficial results of the present study can be ascribed. To directly demonstrate the possible superior efficacy of the present approach, future studies will have to compare the effectiveness of CBT trials for patients screened at risk versus those not at risk, for patients with recent versus longstanding RA, and the application of tailored versus generic or mismatched treatments for RA patients. In addition, treatment effects

were limited to specific indicators of physical, psychological and social functioning and cognitive-behavioral factors. Most evidently, the present trial was unsuccessful in altering primary disease outcomes of pain and functional disability. Previous CBT and self-management trials, usually focusing more exclusively on pain management, have occasionally found effects on pain and functional disability at post-treatment, although these effects were in most cases not maintained at follow-up (e.g., Parker et al., 1995; see also McCracken, 1991; Hawley, 1995; Riemsma et al., 1999, 2002). In the present study, the pain and functional disability module was the least frequently chosen and applied treatment module for only 11 patients, which may be the reason for the lack of effects on these outcomes. A recent RA study also suggests that focusing this treatment module on physiologically mediated changes, such as the use of relaxation and biofeedback in patients with high physiological reactivity to pain, could improve its effects on pain outcomes (Evers et al., 2001b). Moreover, higher expectations of patients in the CBT condition or the greater degree of attention patients in the CBT treatment received might have contributed to the beneficial effects of CBT, requiring expectancy assessments and comparisons with an attention control group in future studies. A selection bias could not be detected in our sample. However, information is unavailable about patients who initially refused to take part in the screening study. To avoid any unmeasured selection bias, the screening procedure should be preferably carried out as part of the standard medical care. Further validation of the empirically derived psychosocial risk profile is also desired, e.g. by comparing questionnaire criteria with standardized interviews for diagnosis of subclinical anxiety and depression. Finally, replication of the effects in larger samples as well as maintenance of treatment effects at longer-term follow-ups, preferably accompanied by cost-effectiveness analyses and use of economic outcome measures - such as health care use, drug intake, and occupational status - is desired to further validate the significance of the findings for application in clinical practice (see e.g., Lorig et al., 1993).

In conclusion, the present study demonstrates that customized treatment for RA patients at risk offered at an relatively early stage of the disease is effective for indicators of physical, psychological and social functioning, and suggests that this approach is a promising way to optimize treatment effectiveness in terms of treatment acceptance and magnitude and maintenance of effects.

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5

Summary

The studies in this thesis were conducted to gain insight into the role of psychological factors in disease outcome for patients with rheumatoid arthritis (RA), a chronic, inflammatory disease affecting the joints. The thesis consists of three main parts, including assessment, prediction and modification of RA disease outcome with psychological factors and tailored treatment. Particular attention was given to factors that are a focus of psychological treatments, including illness cognitions, coping and social support.

ASSESSMENT OF DISEASE OUTCOME: HEALTH DIMENSIONS OF RA

Reliable and valid assessment of disease outcome is a prerequisite to studying the influence of psychological factors and the effects of therapeutic interventions in RA. In addition to the assessment of clinical and laboratory data, health status questionnaires can provide specific, detailed information about health areas that are affected by the disease and that closely reflects functioning and well-being of patients. The goal of the first study in 284 RA patients was to further validate a health status instrument for patients with arthritis, the IRGL, by comparing this inventory to another widely used international health status instrument for arthritis patients, the Dutch-AIMS2 *(chapter 2)*. The IRGL consists of disease-specific scales of physical functioning and disease-generic scales of psychological functioning, social functioning and impact of the disease on daily life. Reliability and validity of the IRGL proved to be highly satisfactory, as indicated by overall high internal consistencies, comparability to the other health status instrument in terms of structure and content of scales, and moderate to high correlations between the physical functioning scales and clinical markers of disease outcome. To facilitate comparisons with the most common, international questionnaire, the AIMS2, regression formulas of the physical and psychological functioning scales were computed between the two questionnaires. In line with previous studies conducted by others, it was concluded that the IRGL is a reliable and valid multidimensional health status instrument for RA patients.

PREDICTION OF DISEASE OUTCOME: RISK FACTORS IN RA

The main aim of this thesis was to examine the role of specific psychological predictors in RA disease outcome, using a prospective design. The predictors studied were based on two theoretical models in accordance with the psychological literature on predicting disease activity and psychological distress in chronic (immune) diseases with stress-vulnerability models, and predicting functional disability and pain in chronic pain disorders with fear-avoidance models. Particular

attention was given to the role of coping, social support, illness cognitions and physiological pain reactivity. Specifically, we studied the role of coping and social support in disease outcome (disease activity, functional disability and pain, psychological distress) after 1, 3 and 5 years in a sample of recently diagnosed patients *(chapters 3.1.1 - 3.1.3).* Of interest was whether coping and social support assessed very early in the disease process, i.e. at the time of diagnosis, would predict short-term changes in RA after 1 year as well as more long-term changes after 3 and 5 years. In addition to these studies conducted among recently diagnosed patients, the role of psychological predictors, not previously assessed in the RA literature, was studied for disease outcome after 1 year in longstanding RA patients: generic illness cognitions and physiological pain reactivity *(chapters 3.2 and 3.3).*

Coping and Social Support

Predictors of disease activity. Based on stress-vulnerability models, the relative contribution of different stressors (major life events and disease-related stressors) and vulnerability factors (personality characteristics of neuroticism and extraversion, stress coping and social support) at the time of diagnosis were studied to predict the course of disease activity after 1, 3 and 5 years in 78 RA patients *(chapter 3.1.1).* Stress-vulnerability factors failed to predict disease activity in the first year after diagnosis, possibly due to the relatively strong effects of medication in the first year. In the longer term, passive avoidance coping predicted a worse course of disease activity at the 3 and 5-year follow-ups, and lower levels of social support predicted a worse course of disease activity at the 3-year follow-up. In line with preliminary findings in longstanding RA, these results underscore the role of passive avoidance coping with stress and lower levels of social support as possible risk factors for longer-term disease activity in RA.

Predictors of functional disability and pain. On the basis of fear-avoidance models, the role of cognitive and behavioral strategies of pain coping and social support at the time of diagnosis was studied to predict functional disability and pain in 91 RA patients in the first year after diagnosis and in 78 RA participants for whom data was available at the 3 and 5 year follow-ups *(chapters 3.1.2.1 - 3.1.2.2).* Results indicated that passive pain coping, specifically avoidance of activity (resting) and catastrophic cognitions of pain (worrying) at the time of diagnosis predicted a worse course of functional disability after 1 and 3 years. In addition, social support marginally predicted a less unfavorable course of functional disability after 1 year and relatively strongly after 3 and 5 years. Social support also predicted less increased pain after 3 and 5 years. As proposed by fear-avoidance models, these findings indicate that pain-related avoidance factors and social resources can have relatively long-lasting effects on physical outcomes for RA patients.

Predictors of psychological distress. Within the framework of stress-vulnerability models, different stressors (major life events and disease-related stressors) and vulnerability factors (personality characteristics of neuroticism and extraversion, stress coping and social support) were assessed at the time of diagnosis to predict the course of psychological distress (anxiety and depressed mood) after 1 year in 91 patients and after 3 and 5 years in 78 patients, for whom follow-up assessments were available *(chapters 3.1.3.1 - 3.1.3.2*). In accordance with findings among longstanding RA patients, about 30% of those with early RA were characterized by heightened levels of psychological distress, comparable to subclinical levels of anxiety and depressed mood. When predicting psychological distress in the first year of the disease, lower levels of social support marginally predicted a more unfavorable course for one indicator of psychological distress - depressed mood - after 1 year. In the longer term, the personality characteristic of neuroticism relatively strongly predicted a worse course of anxiety and depressed mood after 3 and 5 years, underscoring the role of neuroticism for longer-term psychological distress in RA.

Illness Cognitions

A self-report instrument was developed to assess generic, maladaptive and adaptive illness cognitions in different chronic diseases, including RA: cognitions of helplessness, acceptance and perceived benefits as different ways of evaluating the inherently negative meaning of a chronic disease *(chapter 3.2).* Psychometric characteristics of the instrument were studied in 263 patients with RA and 167 patients with multiple sclerosis (MS). The Illness Cognition Questionnaire (ICQ) reliably and validly assessed the illness cognitions of helplessness, acceptance and perceived benefits. Results supported the comparable factor structure of the questionnaire between the chronic diseases as well as the relatively uniform, maladaptive and adaptive function of the cognitions for the concurrent and future disease outcome. Specifically, illness cognitions of helplessness, acceptance and perceived benefits distinctly predicted all indicators of disease outcomes after 1 year (including disease activity, functional disability and pain, psychological distress), with helplessness demonstrating consistently negative relationships and acceptance and perceived benefits positive relationships with a better disease outcome. It was concluded that the ICQ is a reliable and valid self-report instrument for assessing generic, maladaptive and adaptive illness cognitions in different chronic diseases, including RA.

Physiological Pain Reactivity

On the basis of fear-avoidance models, the role of self reported physiological pain reactivity in comparison to cognitive and behavioral factors (passive pain coping) was studied to predict pain after 1 year in a sample of 95 RA patients *(chapter 3.3).* Physiological reactivity to pain, but not the cognitive and behavioral

factors, predicted increased pain after 1 year, suggesting that physiological patterns of autonomic and muscular pain reactivity have detrimental effects on RA pain. A path model revealed that neuroticism affected physiological pain reactivity, which in turn was the only significant predictor for future pain. When analyzing the types of physiological reactions to pain, a different pattern of physiological responses to pain was reported by RA patients than what has been previously been found in other chronic pain patients, possibly suggesting a symptom-specific pattern of physiological pain reactivity in RA patients.

MODIFICATION OF DISEASE OUTCOME: TAILORED TREATMENT IN RA

An intervention study was conducted to explore whether tailoring treatment to patients at risk with early RA is a promising way to optimize treatment effectiveness *(chapter 4)*. Based on the main findings of the prospective studies, it was expected that the effectiveness of psychological interventions for RA patients might be optimized if tailor-made interventions were offered to patients at risk in a relatively early stage of the disease. A randomized, controlled trial with tailor-made treatment modules was conducted with 64 patients with relatively early RA, who had been screened for psychosocial risk profiles. All patients received standard medical care from a rheumatologist and rheumatology nurse consultant. Half of the patients also received an individual cognitive-behavioral treatment (CBT) with two out of four possible treatment modules. Choice of treatment modules was determined on the basis of patient priorities, which resulted in most frequent application of the fatigue module, followed by the negative mood, social relationships and pain/functional disability modules. Results indicated beneficial effects for CBT on physical, psychological and social functioning. Specifically, fatigue and depression were significantly reduced after treatment and at the 6-month follow-up, and perceived support increased at follow-up assessment in the CBT condition in comparison to the control condition. In addition, helplessness decreased at post-treatment and follow-up assessment, active coping with stress increased at post-treatment, and compliance with medication increased at follow-up assessment in the CBT condition in comparison to the control condition. The treatment condition was characterized by relatively low dropout rates and the effects on primary outcomes were overall moderate in size and maintained at follow-up. The current study demonstrates that customized treatment for RA patients at risk offered at a relatively early stage of the disease is effective for indicators of physical, psychological and social functioning and supplies preliminary support for the idea that customizing treatments to patient characteristics may be a way to optimize CBT effectiveness for RA patients.

6

General Discussion

The objective of the studies in this thesis was to gain insight into the role of psychological factors that are relevant to disease outcome of patients with rheumatoid arthritis (RA). The general findings of these studies will be separately discussed for the assessment *(chapter 2)*, prediction *(chapter 3)* and modification *(chapter 4)* of RA disease outcome. The discussion of *chapter 2* includes a discussion of the assessment of both disease outcome and psychological predictors. In the discussion of *chapter 3*, the role of the different psychological predictors and disease characteristics is discussed, followed by a discussion of the limitations of the prospective studies. The discussion of *chapter 4* deals with the screening procedure for patients at risk and the effects of tailored CBT treatment. The chapter ends with a section about recommendations for future research and clinical implications.

ASSESSMENT OF DISEASE OUTCOME: HEALTH DIMENSIONS OF RA

The reliable and valid assessment of disease outcome is a prerequisite for studying the impact of psychological factors and therapeutic interventions. In the first study in this thesis, a health status instrument for patients with arthritis, the IRGL, was further validated for RA patients (*chapter 2).* Results indicated the IRGL's highly satisfactory reliability and validity in terms of high internal consistency, comparability of structure and content of scales to the Dutch-AIMS2, as well as moderate to high relationships between physical functioning scales and clinical and laboratory markers of disease outcome. Other aspects of reliability and validity have previously been studied by others, e.g. concurrent validity of the psychological and social functioning scales, test-retest reliability and sensitivity to change (e.g., Huiskes et al., 1990a,b; Geenen et al., 1995; Kraaimaat et al., 1995b,c; Jacobs et al., 2001). Further data on reliability and validity were obtained in the following studies in this thesis *(chapters 3 - 4).* A slightly adjusted version of the IRGL also proved to be a reliable and valid instrument for multiple sclerosis patients *(chapter 3.2),* demonstrating the advantage of using disease-generic scales for the dimensions of psychological and social functioning. It can be concluded that the IRGL is a useful clinical instrument for screening and evaluating health aspects in patients with RA and possibly also other chronic diseases.

Recent developments in the RA literature have turned attention to a relatively unexplored area of RA disease outcome, i.e. fatigue. Fatigue has only recently received attention as a frequent problem in RA (Belza, 1995; Huyser et al., 1998). Similar to pain, fatigue seems to be affected by both the disease process and psychological factors (Huyser et al., 1998). Taking the small sample size into account, one of the studies in this thesis indicated that fatigue is a high priority

when patients are asked which topic they wanted to deal with in psychosocial interventions *(chapter 4)*, underscoring the role fatigue may play from a patient perspective. Like all health status instruments for arthritis patients, the IRGL does not assess this aspect of physical functioning. However, the intervention study in this thesis *(chapter 4)* suggests that the CIS, a questionnaire validated for various chronic diseases (Vercoulen et al., 1996), is a suitable instrument for assessing fatigue in RA patients. Reliable and valid measurement is obviously as important for psychological predictors. Although not a focal point of this thesis, the studies in this thesis showed sufficient reliability, concurrent and predictive validity for the PCI passive pain coping scales, the UCL passive avoidance stress coping scales, the ICQ illness cognitions scales of helplessness, acceptance and perceived benefits, the physiological pain reactivity scale, and the IRGL social support scales.

In view of the limitations of self-report measures, further validation should focus on the relationships with observed and physiological assessments. For example, comparing the IRGL social support scales to observed social interactions with significant others and daily monitoring of social activities, the PCI passive pain coping scales to observed pain behaviors and electronic activity devices, and the physiological pain reactivity scale to physiological measures of autonomic and muscular reactivity patterns can deliver important information about possible pathways of the predictors to RA disease outcome. To specify dimensions of the IRGL disease outcome, comparisons to qualitative interview assessments (e.g., for subclinical levels of anxiety and depressed mood), observational measurements (e.g., observed assessment of functional disability) and daily monitoring of symptoms (e.g., pain diary assessments) is recommended.

PREDICTION OF DISEASE OUTCOME: RISK FACTORS IN RA

Different studies in this thesis have examined the role of psychological predictors in RA disease outcome, using a prospective design. Based on the main findings of the studies, the psychological predictors (coping, including physiological pain reactivity, social support, illness cognitions, personality characteristics, and stressors) and disease characteristics (stage of disease, duration of effects, specificity for RA) will be separately discussed, followed by a discussion of the limitations of the studies.

PSYCHOLOGICAL PREDICTORS

Coping

Coping can be defined as individuals' behavioral and cognitive attempts to manage or tolerate stress. Two main areas of coping research have been distinguished in RA: coping with stress in general and coping with a specific, disease-related stressor, i.e. pain (see e.g. Manne & Zautra, 1992; Jensen et al., 1991b). Stress-vulnerability models propose that an individual's reaction to stressors in general, including coping with stress, primarily affects the outcome of disease activity and psychological distress. The manner of coping with pain has been assumed to play a major role in functional disability and pain, as supposed in fear-avoidance models. In the present studies conducted with patients with early RA *(chapters 3.1.1 - 3.1.3)* support was found for both models. The passive avoidant strategy of coping with stress (assessing cognitive-behavioral attempts to avoid, escape and acquiesce when facing everyday problems) predicted a worse course of disease activity after 3 and 5 years. Passive coping with pain (assessing cognitive-behavioral factors of avoidance of activity and catastrophic cognitions when faced with pain) predicted a worse course of functional disability after 1 and 3 years, indicating that passive avoidant ways of coping with stress and pain have detrimental effects on longer-term physical health in early RA. Corresponding relationships have previously been found in prospective studies with patients with longstanding RA, patients with chronic pain disorders and other chronic diseases, suggesting that passive coping with stress and pain is a relatively general risk factor for worse health and disease outcomes (see for RA, Brown & Nicassio, 1987; McFarlane et al., 1987; Keefe et al., 1989; Smith & Wallston, 1992; van Lankveld et al., 1999; Scharloo et al, 1999, see for chronic pain, e.g. Jensen et al., 1991b, see for chronic diseases, e.g. Stanton et al., 2001). In contrast, coping did not predict the course of psychological distress in our studies of early RA, possibly indicating that coping is less relevant for longer-term psychological than physical health outcomes.

In line with findings in longstanding RA and other populations, active strategies of coping with stress or pain systematically failed to demonstrate any effects for future disease outcomes. Different reasons have been discussed for this lack of effects. For example, there is some evidence that active coping, together with other concepts supposed to be adaptive, have a stronger predictive capacity for positive outcome measures, such as positive mood, than negative outcome measures, such as anxiety and depression (e.g., Manne & Zautra, 1992; Zautra et al., 1995; Smith et al., 1997; Stanton et al., 2001, see also *chapter 3.2*). The lack of effects for active coping has also been ascribed to a higher context-specificity of adaptive than maladaptive ways of coping (Smith et al., 1997, Stanton et al., 2001). For example, frequent use of active strategies may work beneficially at stages when the disease is relatively nonactive but unfavorably when faced with highly

uncontrollable situations, such as during periods of RA inflammation. It may be consequently necessary to link the effects of active strategies more closely to the characteristics of stressors, particularly the level of controllability.

When considering different stress response systems, coping not only include cognitive and behavioral responses, but also physiological reactions to stressors, such as pain (Flor et al., 1990). In one of the studies in this thesis, the relative contribution of self-reported cognitive, behavioral and physiological reactivity to pain was compared in relation to future pain in longstanding RA *(chapter 3.3).* Results indicated that only self-reported physiological reactivity to pain predicted subsequent pain, suggesting detrimental effects of physiological patterns of autonomic and muscular pain reactivity on RA pain. Together with the findings in early RA that cognitive and behavioral pain responses (passive pain coping) predicted solely future functional disability, and not future pain *(chapters 3.1.2.1 - 3.1.2.2),* the results suggest that specific outcomes in chronic pain patients are predicted by specific cognitive, behavioral and physiological factors. These results also support the view that coping research might benefit from the systematic comparison of the cognitive, behavioral and physiological response systems to clarify their effects on disease outcomes, to specify the underlying processes responsible for these effects, and to identify the most active treatment components (cf. Flor et al., 1990, Turk & Flor, 1999).

Social Support

The most common conceptualization of social support comprises qualitative and quantitative indicators, including aspects of perceived availability of support and size of the social network (Cohen & Wills, 1985; Wills & Fegan, 2001). In accordance with findings in longstanding RA, other chronic diseases and the general population (see Wills & Fegan, 2001), these social support indicators relatively consistently predicted a less unfavorable disease outcome in early RA: less disease activity after 3 years, less functional disability after 1, 3 and 5 years, less pain after 3 and 5 years and less depressed mood after 1 year *(chapters 3.1.1 – 3.1.3),* suggesting that social support is a relatively general protective factor for future RA disease outcome. Effects of social support have previously been studied in RA patients over a period of 1 year or less. In our studies, social support, particularly the perceived availability of support, demonstrated the strongest effects at the later 3 and 5-year follow-ups on physical health outcomes. Together with findings in the general population showing that social support can have long-term physical benefits and decrease mortality rates (see Wills & Fegan, 2001), results suggest that the significance of social support for future physical health outcome have been underestimated in previous RA research.

Illness Cognitions

As for coping, little is known about possible adaptive cognitive reactions when patients are faced with uncontrollable, long-term stress of a chronic disease. There is increasing evidence from prospective studies that cognitive attempts to control uncontrollable circumstances may work maladaptive in the long-term (cf. Stanton et al., 2001). It was assumed that illness cognitions showing consistently favorable effects should focus on the (re)evaluation of the negative meaning of a chronic disease instead on perceived control. A self-report instrument, the Illness Cognition Questionnaire (ICQ) was developed to assess maladaptive and adaptive disease-generic illness cognitions of helplessness, acceptance and perceived benefits in various chronic diseases, reflecting different ways of evaluating the negative meaning of a chronic disease *(chapter 3.2)*. Results in patients with RA and MS indicated a high degree of correspondence between both diseases, in terms of factor structure and concurrent and predictive validity. The cognitions also separately predicted all future disease outcomes, including disease activity, functional disability and pain and psychological distress, with helplessness demonstrating consistently negative relationships and acceptance and benefits positive relationships to a better disease outcome. Although findings have to be replicated, results support the idea that there are generic maladaptive and adaptive cognitions that demonstrate relatively uniform effects when patients are confronted by a chronic disease.

The predictive value of these cognitions for different indicators of disease outcome and the relatively general assessment may suggest that illness cognitions at least partly mediate the effects of coping and social support to future disease outcomes (e.g. Leventhal et al., 1984). The relative impact of illness cognitions, coping and social support has not been assessed in the present study. However, a prospective study in RA have shown that, although illness cognitions of helplessness, passive coping and social support affected each other, they made all a unique contribution to future outcomes (Smith & Wallston, 1992), underscoring the distinct function of illness cognitions, coping and social support.

Personality Characteristics

Two personality characteristics of the Big Five, supposed to be most relevant to physical and psychological health outcomes in the general population and patients with chronic diseases, including RA, have been studied in the present studies: neuroticism and extraversion.

Neuroticism or negative affectivity is assumed to be a generic, underlying factor for psychological risk factors and to possibly account for the effects of illness cognitions, coping and social support on long-term outcomes (e.g., Watson & Pennebaker, 1989; McCrae, 1990). In the present studies, the role of neuroticism has been studied in relation to all disease outcome parameters *(see chapters 3.1-3.3)*. Corresponding to findings among patients with longstanding RA (see e.g.,

Affleck et al., 1992, 1994; Smith et al, 1995), neuroticism did not substantially predict future physical health outcomes, such as disease activity, functional disability or pain, but proved to be a relatively strong predictor for psychological distress in the longer term in early RA. This finding is consistent with research in the general population, showing that neuroticism is a common risk factor for psychological distress (see Clark et al., 1994). However, neuroticism did not greatly account for the relationships of psychological risk factors to future disease outcomes in any of the studies in this thesis. Although neuroticism was related to most of the psychological predictors, it did not largely explain their relationship to future RA disease outcome, indicating that illness cogntions, coping, and social support made a specific, additional contribution to predicting longer-term health (see also Affleck et al., 1992, 1994; Stanton et al., 2001). An example of how neuroticism may indirectly affect future disease outcome was revealed in the study of physiological pain reactivity *(chapter 3.3):* a path model indicated that neuroticism predicted physiological reactivity to pain, which in turn was the only predictor of subsequent pain. Together, these results may support the role of neuroticism in precipitating specific risk factors, which for their part contribute to unfavorable health effects.

In contrast to neuroticism, extraversion has received far less attention in the health and chronic diseases literature (see e.g., Phillips & Gatchel, 2000). In the present studies in patients with early and longstanding RA *(chapters 3.1.1 - 3.1.3, 3.2),* there were no predictive effects for extraversion found for future disease outcomes in early RA. Extraversion was also not more than modestly related to illness cognitions, coping and social support, suggesting that the predictors are hardly affected by the tendency to be more impulsive and sociable. Overall, these results suggest that extraversion does not play a major role as a predictor of future RA disease outcomes or as factor underlying illness cognitions, coping, and social support.

Stressors

Stressors are considered as important predictors for disease outcome in RA, particularly due to the supposed link between stress and inflammatory activity via immunological pathways (see Huyser & Parker, 1998; Walker et al., 1999). Early stress research has mainly focused on major life events, while chronic disease-related stressors have received less attention. In line with stress-vulnerability models, the contribution of both types of stressors was studied in this thesis for disease activity and psychological distress in the first years of the disease *(chapters 3.1.1 and 3.1.3).* Results generally failed to demonstrate any direct, mediating or moderating effect of these stressors on longer-term disease outcome. Consistent with RA research, demonstrating only incidentally relationships between for example major life events and RA disease outcome (see e.g., Potter & Zautra, 1997; Dekkers et al., 2001), results suggest that these stressors do not play a major

role in RA. However, there is some evidence for relationships between specific stressors and future disease activity or immunological parameters in RA patients. Particularly minor and interpersonal stressors, not assessed in the present studies, have previously been shown to be concurrently or prospectively related to disease activity and immune functioning and may be an important additional factor in relation to how stress might affect RA disease activity in the long-term, directly or as a modifying factor for illness cognitions, coping and social support (Affleck et al., 1997; Potter & Zautra, 1997; Zautra et al., 1997, 1998).

DISEASE CHARACTERISTICS

Stage of the Disease

Early detection and modification of psychological risk factors is by definition more likely to have long-term benefits and decrease unfavorable long-term disease outcome in a chronic disease, such as RA. One of the purposes of the thesis was to study whether psychological risk factors at the earliest point in time - at diagnosis – could predict future RA disease outcome and if so, whether corresponding relationships would be found than in longstanding RA *(chapters 3.1.1 - 3.1.3)*. Results indicated that psychological risk factors, such as coping, social support and personality characteristics, at the time of diagnosis predict the course of all indicators of the disease outcome, including disease activity, functional disability and pain and psychological distress. The specific psychological factors and direction of effects correspond to findings in longstanding RA, suggesting that the same psychological mechanisms are involved in early RA as at a later stage of the disease. The early manifestation of these factors at the time of diagnosis suggests that they at least partly result from prior learning histories or predisposition and that RA may have been the factor that has elicited or activated them.

Conclusions about factors specific to the first stage of the disease have to be drawn with caution, since there were no comparative studies conducted with patients with longstanding RA in the thesis. However, there are some indications for specific effects in the first year of the disease. The nonsignificant or slight contribution of psychological predictors to disease activity and psychological distress in the first year after diagnosis and the relatively great improvements in clinical status during this year, probably due the beneficial effects of the RA second-line medication (van Jaarsveld et al., 2000; van Everdingen et al., 2002), suggest that the effects of some psychological predictors may be overshadowed by medication effects in the first stage of the disease *(chapters 3.1.1 and 3.1.3.1)*.

The fact that psychological predictors generally seem to have about the same relationship to future outcomes in early and longstanding RA does not imply that psychological risk factors do not change during the disease process. There is some support that psychological factors are affected by the inflammatory processes of

the disease, its biopsychosocial consequences and pharmacological treatment with prolonged medication (van Lankveld et al., 1993; Fex et al., 1998; van Jaarsveld et al., 1998, 2000; Penninx et al., 1999; Jacobs et al., 2001). However, changes of psychological predictors were not a primary goal of the present study, i.e. the present studies did not compare specific predictors in patients with early and longstanding RA nor were predictors assessed over periods longer than 1 year. Repeated assessments of predictors over longer time periods are warranted to get more insight into possible changes of psychological predictors during the course of RA.

Duration of Effects

There is some support in the general population that factors, such as social support, can have lasting effects on physical health outcomes (Wills & Fegan, 2001). For patients with RA, psychological predictors have hardly been studied for periods longer than 1 year. One purpose of the present studies was to examine whether psychological factors affect disease outcome after 3 and 5 years in patients with early RA and whether relationships may differ between short-term and long-term outcomes *(chapters 3.1.1 - 3.1.3).* It was assumed that more generic and stable predictors than specific disease-related predictors might affect longer-term changes. In addition, the strength and direction of relationships between psychological predictors and future outcomes was assumed to be possibly different for short- and long-term outcomes.

Results indicated that the personality characteristic of neuroticism, passive coping with stress and pain and social support predicted RA disease outcome after 3 and 5 years. Long-term effects after 5 years were found for the relatively generic predictors of neuroticism, passive coping with stress and social support. More disease-related predictors of passive coping with pain were only significant up to 3 years after diagnosis, possibly due to changes brought about by the disease and physical symptoms itself. In addition, the strength of effects for coping with pain was somewhat reduced after 3 years, while delayed or increased effects were overall found for the more generic predictors of neuroticism, stress coping and social support (in relationship to the physical outcomes) after 3 and 5 years. Effects were in line with previous studies in longstanding RA over shorter periods of time and no evidence was found that direction of effects changed during the study period. In addition to these results in our studies, long-term effects of illness cognitions of helplessness on RA disease outcome over a period of 4 years have previously been reported (Smith et al., 1994). Overall, the findings suggest that psychological factors, particularly the more generic predictors of personality characteristics, stress coping, and social support, can have lasting effects on RA disease outcome.

Specificity for RA

In the present studies, we used theoretical models and validated findings from the general population and populations with chronic pain and chronic (autoimmune) diseases, which were assumed to be applicable to RA patients. The stress-vulnerability and fear-avoidance models appeared to be useful approaches to predicting RA disease outcome. Although only some of the hypothesized effects were found, direction of the significant effects for personality characteristics, illness cognitions, coping and social support all corresponded to theoretical models and empirical findings in the general population, populations with chronic pain disorders or other chronic diseases. It may be concluded that general psychological factors, such as neuroticism, passive coping with stress and pain, social support and helplessness, affect disease outcome similarly in RA as in a wide range of populations (cf. Steptoe, 1991a).

The fact that about the same relationships were found as in patients with other chronic diseases and chronic pain disorders does not imply that underlying mechanisms are the same in different populations. The mechanisms linking these factors to disease outcome and the kind of modification procedures necessary to change the psychological predictors are still scarcely understood. In addition, psychological predictors do not always work in the same direction in various populations, such as patients with different immune diseases. For example, the detrimental effects for passive avoidant stress coping on disease activity in early RA *(chapter 3.1.1)* are in line with general findings of longer-term effects of avoidance factors in the general population (see e.g., Suls & Fletcher, 1985; Stanton et al., 2001) and have also been found on future disease activity in cancer patients (Epping-Jordan et al., 1994). However, effects of passive avoidance in the other direction, i.e. more avoidance predicted decreases of future disease activity and immunological functioning, have been reported for the immune disease HIV (Mulder et al., 1999), demonstrating how complex the underlying mechanisms of relationships between psychological predictors and future disease and immunological outcomes in different populations might be. In this thesis, possible disease-specific effects for RA patients were found in the study on physiological pain reactivity *(chapter 3.3),* in which a different pattern of physiological responses to pain was reported by RA patients than what has been previously been found in heterogeneous groups of chronic pain patients (McCracken et al., 1996), suggesting a specific pattern of physiological reactivity to pain in at least subgroups of RA patients. Further study of the underlying mechanisms of these effects in different populations of chronic diseases and chronic pain is necessary to gain more insight into possible disease-specific relationships between psychological factors and RA disease outcome.

LIMITATIONS OF THE PROSPECTIVE STUDIES

Generalizability of Findings

When studying the significance of specific risk factors in a population, a prerequisite for the generalizability of the findings is the representativeness of the study samples. Representativeness in prospective research is threatened by the initial inclusion of patients and subject dropout over time. Comparisons of demographic variables and disease outcome parameters with representative samples with early and longstanding RA indicated that the characteristics of our study samples were all highly comparable to the norm samples. However, the following selection bias may still have affected our samples. Patients were recruited from different university and general rheumatology outpatient clinics. Results might consequently not be applicable to patients under treatment in general practices, possibly limiting the findings of the present studies to patients with more severe RA. Patients with early RA also participated in a clinical protocol. In addition, dropouts scored somewhat higher on neuroticism and psychological distress in the studies on early RA *(chapters 3.1.1-3.1.3).* Due to the fact that neuroticism and psychological distress are related to most of the psychological predictors, our findings may be limited to patients characterized by moderate levels of psychological risk factors. However, this state of affairs might have also led to an underestimation of their effects in the patients with early RA. In patients with longstanding RA, there were no differences found between dropouts and participants after 1 year (these analyses are not reported in the studies in *chapter 3.2* and *chapter 3.3*).

Threats to Internal Validity

When monitoring a population over longer periods of time in a natural setting, conclusions about possible causal relationships between the predictors and the outcome are threatened by internal validity. That is, other biomedical and psychological variables not measured in the study may have affected the course of disease outcome and contributed to the relationships found, such as variables related to the disease process itself, its (pharmacological) treatment and biopsychosocial consequences. In the present study, possible relevant confounding variables were taken into account, such as demographic variables, clinically assessed outcomes of disease activity, neuroticism and, in the study on patients with early RA, also pharmacological treatment. However, we cannot exclude the possibility that additional treatments or other biomedical factors supposed to affect future RA disease outcome (e.g., continuing physical therapies) to some extent account for the relationships found.

Statistical Analyses

It may be argued that, by using regression analyses, mainly the contribution of single factors to specific disease outcome parameters was studied, without testing more complex models in Structural Equation Modeling (SEM). One main advantage of SEM models is that the relationship between several predictors and different disease outcome parameters can be simultaneously analyzed. One example has been applied in the study of physiological pain reactivity in which neuroticism affected physiological pain reactivity which in turn predicted subsequent pain *(chapter 3.3).* However, the relatively small sample sizes in our prospective studies allowed only testing of very limited SEM models. Relationships between predictors were further explored in regression analyses by examining mediator and moderator effects in patients with early RA *(chapters 3.1.1 – 3.1.3).* Results indicated that the different predictors almost all independently predicted future disease outcome, and no mediator effects were revealed with one exception (i.e. a mediating effect of neuroticism and educational level for the relationship between functional disability and anxiety after 5 years, *chapter 3.1.3.2*). Moderator analyses between the predictors were also relatively extensively studied, expecting for example that the detrimental health effects of more passive coping and lower levels of social support could increase in patients scoring higher in neuroticism or confronted with higher stressor levels. However, the results of our studies failed to support any moderating function of the predictors for changes in RA disease outcome.

MODIFICATION OF DISEASE OUTCOME: TAILORED TREATMENT IN RA

Main findings of the prospective studies suggest that effectiveness of psychological interventions for RA patients may increase when applying tailored treatment to patients at risk at a relatively early stage of the disease. Consequently, a randomized, controlled trial with tailor-made treatment modules was conducted among patients with relatively early RA who had been screened for psychological risk profiles *(chapter 4).* Although results from this study were generally promising, limitations regarding the selection of patients at risk and interpretation of findings have to be considered.

SCREENING FOR PATIENTS AT RISK

A prerequisite for the application of tailored treatment for patients at risk is the use of validated screening instruments. Based on the findings of the prospective studies

(chapter 3), indicators of illness cognitions, coping and social support that predicted future RA disease outcome were included in the screening procedure. Heightened distress was chosen as the main criterion, due to the fact that it is the most comprehensive indicator of the risk factors. At risk was consequently defined as heightened psychological distress together with at least two out of six psychological risk factors, using previously determined cutoff scores from the prospective studies. Although these criteria were empirically derived, the validity of this approach has to be investigated by future research. For example, statistical findings relate to group findings and the extent to which the instrument screens individual patients in the right category has to be validated, e.g. by comparing results to other selection methods, such as structured interview assessments, and monitoring screened patients over time. It has to be noted that no a priori, categorical distinction exists between patients at risk and those not-at risk, since the screening instrument used continuous variables for predicting linear relationships of the outcome parameters, and an individual only has a relative risk of a more or less unfavorable disease outcome. For these reasons, cutoff criteria are to some extent artificial boundaries and individuals scoring around the cutoff scores have the greatest chance of being incorrectly categorized. It is consequently preferable to use screening instruments as a first general selection, followed by more extensive assessments, even when reliability and validity of the instruments have been shown to be high.

TAILOR-MADE CBT FOR PATIENTS AT RISK

Results of the CBT trial revealed that tailored treatment offered to patients at risk at a relatively early stage of the disease was effective for indicators of physical and psychological functioning and psychological risk factors. The effects on primary outcomes of fatigue and depression were of a moderate magnitude with effect sizes of approximately .50, comparable to effect sizes found in meta-analyses for gold injections on RA swollen joints (Clark et al., 2002). Magnitude of these effects was maintained at the 6-month follow-up. The treatment condition was also characterized by relatively low dropouts rates (6%), suggesting high treatment acceptance of tailored treatment. It was concluded that, in comparison to findings of recently conducted RA meta-analyses (Hawley, 1995; Riemsma et al., 2002), offering tailor-made treatment to patients at risk may be a promising way to optimize RA treatment effectiveness in terms of treatment acceptance, and magnitude and maintenance of effects.

Although results were generally promising, several limitations of the study have to be considered. Most importantly, the hypothesis that tailored CBT for patients at risk at an early stage of the disease may be superior to general CBT treatments for all RA patients was not tested in the present trial. Comparisons to

other trials are problematic due to differences between studies in type of intervention, control groups, designs, outcome measures and settings. To directly demonstrate the superior efficacy of the present approach, it is necessary to compare the effectiveness of CBT trials for patients screened at risk versus those not at risk, for patients with recent versus longstanding RA, and the application of tailored versus generic or mismatched treatments. In addition, treatment effects were limited to specific indicators of disease outcome and psychological risk factors. Most evidently, the trial was unsuccessful in altering primary disease outcomes of pain and functional disability, although effects on these outcomes have incidentally been found in other CBT and self-management trials with RA patients (see Hawley, 1995). The lack of effects in our study may be due to a lack of statistical power, since the pain and functional disability module was less frequently applied than the other treatment modules. In addition, our study on physiological pain-reactivity suggests *(chapter 3.3)* that it may be beneficial to focus this treatment module on physiologically mediated changes, such as the use of relaxation and biofeedback in patients with high physiological reactivity to pain. Finally, replication of the treatment effects in larger samples with longer-term follow-ups, preferably accompanied by cost-effectiveness analyses and use of economic outcome measures, such as health care use and drug intake, is warranted.

FUTURE RESESARCH

In addition to validating the tailored intervention approach, future research should primarily focus on underlying mechanisms of the psychological predictors identified in the prospective studies, studying physiological, cognitive, behavioral and social pathways of the predictors in relationship to RA disease outcome. Possible relevant concepts, not assessed in the studies of this thesis, are discussed below.

Fear-avoidance models assume that beliefs about pain-related fears and hypervigilance mediate or precipitate the relationship of avoidance of activity and catastrophic pain cognitions to functional disability in chronic pain patients (see e.g., Vlaeyen & Linton, 2000). Both concepts have been shown to be possibly relevant for patients with RA (McDermid et al., 1996; Strahl et al., 2000). However, specific pain-related fears identified in other chronic pain populations, such beliefs about fear of movement or reinjury, might not apply to RA inflammatory pain with irreversible joint damage. For the possible application of recently developed treatments of exposure in vivo in chronic pain patients for patients with RA (Vlaeyen et al., 2001), it is necessary to clarify specific pain-related fears of patients with RA. In addition, physiological fear reactions or hypervigilance to pain may contribute to the effects of the self-reported

physiological pain reactivity for future pain outcomes. Simultaneous assessment of physiological and self-reported autonomic and muscular reactions can clarify the extent to which self-reported physiological reactivity is based on specific cognitive or physiological mechanisms. In the event that a physiological basis is supported, modification procedures aimed at altering autonomic and muscular reactivity, such as relaxation and biofeedback, may be applied to RA patients with high physiological pain reactivity. Finally, future research has to clarify the possible mediating function of physical deconditioning processes and decreased muscle strength for the relationship between pain-related avoidance factors and long-term pain outcomes (Dekker et al., 1993b; Steultjens et al., 2002).

Several pathways may be responsible for the relationship of avoidance coping with stress to RA disease activity. At a cognitive-behavioral level, there is some support that an avoidant coping style in daily life lead to less compliance with medication prescriptions and less adherence to recommendations of health care providers (Sherbourne et al., 1992), possibly accompanied by cognitive processes, such as a lack of attention to bodily signals, such as pain, or denial of physical signs of inflammation (cf. Steptoe, 1991a). An avoidant coping style may be also linked to a lack of processing or expressing affective information, in line with previous beneficial effects found for emotional disclosure interventions on RA disease activity (Smyth et al., 1999). Finally, physiological pathways, particularly the way in which avoidance affects immunological functioning, should have priority, in light of empirical findings showing that avoidance is related to future disease activity in different immune diseases (Epping-Jordan et al., 1994; Mulder et al., 1999).

The predictive value of social support for various physical disease outcomes in early RA in the longer-term suggest that social support may be linked to a broad range of cognitive, behavioral and physiological reactions to stress and pain (see e.g. Wills & Fegan, 2001). Different mechanisms may be responsible for the various health effects. For example, stimulation of social activities and health-related coping assistance by significant others may decrease functional disability, while more favorable immune functioning due to emotional support might be a pathway to reduced disease activity. Possible physiological mediators of social support have been studied in the general population, particularly immunological pathways, and there is relatively convincing evidence that social support indicators, such as the size of the social network and perceived support, are related to immunological and neuroendocrine variables (see Kiecolt-Glaser et al., 2002; Uchino et al., 1996). Social support have also been linked to different cognitive-behavioral pathways, such as more information seeking and cognitive restructuring, higher activity levels and less pain behaviors (Manne & Zautra, 1989; Jamison & Virts, 1990). Finally, relationships between interpersonal stressors and disease activity (Potter & Zautra, 1997; Zautra et al., 1997) as well as the modifying effects of social support on this relationship in RA (Zautra et al.,

1998) underscore the importance of studying different supportive and problematic social aspects in combination with cognitive-behavioral and physiological mediators.

The conceptualization of acceptance and perceived benefits as adaptive illness cognitions in the face of a chronic disease warrants further validation. It can be supposed that the adaptive function of these cognitions varies when individuals are confronted by different long-term stressors. To get more insight into the function of these cognitions, their predictive value for disease outcomes should be compared to control-related cognitions, such as perceived control or self-efficacy, when faced with long-term stressors that differ in degree of controllability, chronicity or predictability (see e.g., Felton & Revenson, 1984). In addition, underlying mechanisms need to be better understood. For example, recent theoretical and empirical approaches suggest that, when individuals are faced with uncontrollable long-term stress, acceptance may be related to lowered autonomic and muscular reactivity, fewer attempts to solve unsolvable problems by excessive worrying and an extremely active coping style, as well as higher ability to cognitively restructure primary goals and goal setting (e.g., McCracken et al., 1998; Risdon et al., 2003). Research may finally lead to the development of specific modification procedures that foster adaptive cognitions in the face of uncontrollable long-term stress. Modification procedures for acceptance may for example consist of stimulating processes of loss, exposure to the situation of being chronically ill in the case of high avoidance, cognitive restructuring of life goals and problem-solving capacities for mastering unavoidable, negative consequences in daily life.

CLINICAL IMPLICATIONS

The present studies were conducted to gain more insight into psychological factors affecting RA disease outcome to enable the development of more effective therapeutic interventions. One main conclusion of the present studies is that specific psychological factors, such as illness cogntions, coping and social support, can affect longer-term RA disease outcome, underscoring the significance of multidisciplinary RA treatment approaches. More importantly, preliminary support was provided for the idea that customizing treatments to patient characteristics, in terms of patient selection and types and timing of treatment, may optimize treatment effectiveness. Specifically, results suggest that tailor-made treatment for patients at risk at an early stage of the disease may be a promising way to improved effectiveness of psychological interventions in RA. In addition to the preliminary empirical support provided in this thesis, this approach seems to closely correspond to clinical considerations. For example, offering psychological treatment to

patients at risk is in line with the clinical views of rheumatologists and nurses that psychological factors may play a role primarily in subgroups of patients. Tailor-made treatment is supposed to better match patients' needs and may increase patient satisfaction and compliance, while early detection, diagnosis, and treatment offers a better chance of decreasing unfavorable long-term disease outcomes.

Reliable and valid screening is a prerequisite to using a tailored treatment approach for patients at risk. Self-report questionnaires can supply relatively objective information and assist rheumatologists and nurses in their decisions about clinical referral and supplementary treatments options. The use of screening instruments may be especially relevant for risk factors that are usually not part of regular clinical care, such as the way in which patients cope with problems of daily life or their social support system. The present screening procedure can be viewed as a promising, empirically based approach, but its reliability, validity and practicability has to be further supported. Due to treatment decisions for individual patients, it has to be considered that screening instruments are preferably used as an initial general selection, followed by more extensive assessments, such as standardized interviews.

Questions may ultimately arise about the possibility of implementing and integrating tailored treatment in standard rheumatology care. Although empirically based conclusions can not be drawn, given the present state of research, recent developments in multidisciplinary treatment approaches seem to offer possibilities for tailored approaches in clinical practice. For multidisciplinary teams of rheumatology care (including e.g., rheumatology consultants, physical and occupational therapists, psychologists), it may be a fruitful to offer stepwise additional treatment options, depending on the type, number and magnitude of the patients' biomedical and psychological risk factors. For example, offering education about biomedical and psychological risk factors to all patients, self-management group treatment for patients with a relatively aggressive disease course to optimally manage the consequences, and tailored CBT treatment for patients characterized by psychological risk profiles.

7

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Samenvatting

Reumatoïde artritis (RA) is een chronische aandoening die gekenmerkt wordt door ontsteking van de gewrichten. De ontstekingen gaan gepaard met functionele bewegingsbeperkingen, gewrichtspijn en vermoeidheid en kunnen op den duur leiden tot onherstelbare gewrichtsbeschadiging en invaliditeit. De lichamelijke klachten kunnen talrijke beperkingen in het dagelijks leven tot gevolg hebben, zoals beperkingen in het uitvoeren van dagelijkse activiteiten, verminderde sociale contacten, afhankelijkheid van anderen, arbeidsongeschiktheid of financiële gevolgen.

Vanaf de jaren 50 vindt er onderzoek naar psychologische factoren bij RA plaats. In de beginjaren heeft het onderzoek zich gericht op de rol van psychologische factoren voor het *ontstaan* van RA, zonder dat hiervoor ondersteuning werd gevonden. Vanaf begin jaren 80 vond er een verschuiving van de aandacht plaats naar het *beloop* van RA. In deze onderzoekslijn kregen de gevolgen van RA voor het dagelijks leven (kwaliteit van leven), hoe patiënten met deze gevolgen omgaan (bijv. coping en sociale steun), en hoe deze factoren op hun beurt het ziektebeloop kunnen beïnvloeden, meer aandacht. Ook werd de effectiviteit van psychologische interventies, zoals zelfredzaamheidtrainingen en cognitieve gedragstherapie, onderzocht. Hoewel in sommige interventie studies positieve effecten werden gevonden blijkt uit recent uitgevoerde meta-analyses dat de effecten klein en van korte duur zijn. De beperkte effectiviteit van psychologische interventies voor patiënten met RA was aanleiding voor de studies in dit proefschrift. Het doel van dit proefschrift was om meer inzicht te krijgen in de rol van psychologische factoren voor het ziektebeloop bij RA, om van daaruit meer doelgerichte en effectieve interventies te kunnen ontwikkelen.

Het proefschrift bestaat uit drie onderdelen die betrekking hebben op het meten *(hoofdstuk 2)*, voorspellen *(hoofdstuk 3)* en beïnvloeden *(hoofdstuk 4)* van het ziektebeloop bij RA. In hoofdstuk 2 wordt onderzoek beschreven naar de betrouwbaarheid en validiteit van een vragenlijst die verschillende gezondheids-dimensies bij RA vast stelt. In hoofdstuk 3 wordt verslag gedaan van een aantal studies waarin de invloed van psychologische factoren op het ziektebeloop (ziekteactiviteit, lichamelijk en psychisch functioneren) werd onderzocht. Aandacht kregen vooral ziektecognities, coping en sociale steun omdat deze factoren een aangrijpingspunt vormen voor psychologische interventies. Deze factoren kunnen worden omschreven als gedragsfactoren die weergeven welke ideeën en opvattingen patiënten over hun ziekte hanteren (ziektecognities), hoe patiënten omgaan met stress in het dagelijks leven (stress coping) en met ziekte-gerelateerde factoren, zoals pijn (pijn coping), en in welke mate patiënten steun

ervaren vanuit hun sociale omgeving (sociale steun). Op basis van de resultaten uit hoofdstuk 3 wordt in hoofdstuk 4 een 'tailor-made' behandeling geëvalueerd. Onder 'tailor-made' wordt in deze context verstaan dat - in plaats van een algemene behandeling voor alle RA patiënten op een willekeurig moment – een op de patiënt afgestemde behandeling voor een geselecteerde groep patiënten in een bepaalde fase van de ziekte wordt aangeboden.

METING VAN HET ZIEKTEBELOOP: GEZONDHEIDSDIMENSIES BIJ RA

Om de invloed van psychologische factoren en interventies op het ziektebeloop te kunnen onderzoeken, dienen de verschillende aspecten of dimensies van het ziektebeloop betrouwbaar in kaart te worden gebracht. In aansluiting op meer-dimensionale definities van de gezondheidstoestand bij RA, zijn er minimaal drie dimensies te onderscheiden: ziekteactiviteit, lichamelijk en psychisch functioneren.

Ziekteactiviteit reflecteert het meest direct het pathofysiologische proces en wordt doorgaans gemeten met klinische en laboratoriummaten, zoals gewrichtsscores en bloedbezinking. De dimensie van het lichamelijk functioneren omvat de fysieke klachten die gepaard gaan met het ontstekingsproces, zoals functionele bewegingsbeperkingen, pijn en vermoeidheid. De mate waarin patiënten beperkingen in het dagelijks leven ervaren als gevolg van de lichamelijke klachten wordt weerspiegeld in het psychisch functioneren of de psychische distress die patiënten ervaren. De meest gebruikelijke manier om het psychisch functioneren vast te stellen is door angst en depressieve stemming van patiënten te meten.

In tegenstelling tot de ziekteactiviteit worden de dimensies van het lichamelijk en psychisch functioneren doorgaans met vragenlijsten gemeten. In de loop der jaren zijn er verschillende instrumenten ontwikkeld om de gezondheidstoestand van patiënten met reuma in kaart te brengen, zoals bijvoorbeeld de IRGL. Het doel van de eerste studie *(hoofdstuk 2)* was om de betrouwbaarheid en validiteit van de IRGL te vergelijken met een internationale vragenlijst, de AIMS2. Beide instrumenten brengen de dimensies van het lichamelijk en psychisch functioneren in beeld, plus een aantal andere dimensies, zoals het sociaal functioneren en de gevolgen van de aandoening voor het dagelijks leven. Bij 284 RA patiënten werden beide vragenlijsten afgenomen en een aantal klinische en laboratoriummaten bepaald. Uit de resultaten bleek dat de vragenlijsten een vergelijkbaar hoge mate van betrouwbaarheid en validiteit hebben. De validiteit werd ondersteund door hoge samenhangen tussen de corresponderende schalen van de twee vragenlijsten en modale tot hoge samenhangen tussen de schalen voor lichamelijk functioneren en de klinische en laboratoriumbepalingen. Er werd

geconcludeerd dat, in aansluiting op eerder verricht onderzoek, de IRGL een betrouwbare en valide vragenlijst is om de gezondheidstoestand van patiënten met RA in kaart te brengen.

PREDICTIE VAN HET ZIEKTEBELOOP: RISICOFACTOREN BIJ RA

Er zijn aanwijzingen dat psychologische factoren van invloed kunnen zijn op de verschillende dimensies van het ziektebeloop bij RA. Het onderzoek naar predictoren voor het ziektebeloop is gebaseerd op twee modellen die zijn afgeleid van modellen bij chronische (auto)immuun ziekten, chronische pijn aandoeningen en andere chronische aandoeningen: stress-vulnerabiliteit-modellen en fear-avoidance modellen.

Stress-vulnerabiliteit modellen bij chronische (auto)immuun ziekten en andere chronische aandoeningen trachten voornamelijk de ziekteactiviteit, respectievelijk het psychisch functioneren, te voorspellen. Deze modellen veronderstellen dat het ziektebeloop wordt beïnvloed door externe stressoren, zoals ingrijpende stressvolle levensgebeurtenissen ('major life events'), en interne vulnerabiliteitsfactoren, zoals relatief stabiele persoonlijkheidskenmerken. Ziektecognities, stress coping en sociale steun kunnen als additionele vulnerabiliteitsfactoren worden beschouwd. Deze factoren hebben op hun beurt ook een invloed op de relatie tussen stressoren en persoonlijkheidskenmerken en het ziektebeloop. Zo wordt bijvoorbeeld verondersteld dat de invloed van stressvolle gebeurtenissen op het psychisch functioneren mede wordt bepaald door de manier hoe iemand met stress omgaat (stress coping).

Fear-avoidance modellen kunnen als een verbijzondering van stress-vulnerabiliteit modellen worden gezien. In fear-avoidance modellen worden uitspraken gedaan over de rol van psychologische factoren bij een bepaalde stressor, namelijk pijn, om vooral het lichamelijk functioneren bij chronische pijn aandoeningen te voorspellen. Fear-avoidance modellen veronderstellen dat specifieke vermijdingsfactoren in reactie op pijn het lichamelijk functioneren ongunstig beïnvloeden. Deze vermijdingsfactoren bestaan voornamelijk uit het vermijden van activiteiten bij pijn, catastroferende gedachten over pijn, en fysiologische (vooral autonome en musculaire) reacties op pijn. Een tekort aan sociale hulpbronnen of steun, zoals een klein sociaal netwerk of een geringe mate van ervaren steun, worden verondersteld de vermijdingsfactoren te bevorderen en probleemoplossingvaardigheden te belemmeren waardoor pijn en functionele bewegingsbeperkingen in stand worden gehouden of toenemen.

Onderdelen van deze modellen werden in een aantal prospectieve studies van dit proefschrift bestudeerd bij patiënten met RA. Aandacht werd vooral besteed aan de rol van ziektecognities, coping, sociale steun en fysiologische pijn-

reactiviteit. In de eerste vijf studies werd de rol van coping (met stress en pijn) en sociale steun onderzocht voor het ziektebeloop (ziekteactiviteit, lichamelijk en psychisch functioneren) na 1, 3 en 5 jaar bij recent gediagnosticeerde RA patiënten. Er zijn aanwijzingen dat coping en sociale steun het korte-termijn ziektebeloop van ongeveer 1 jaar bij patiënten met langdurige RA kunnen voorspellen. Om meer doelgerichte psychologische interventies te kunnen ontwikkelen is het van belang om vast te stellen of deze factoren het ziektebeloop reeds in een vroeg stadium van de ziekte en over langere periodes dan 1 jaar voorspellen. Het doel van de studies was om vast te stellen of coping en sociale steun in een zeer vroeg stadium van de ziekte, ten tijde van de diagnose, het korte termijn ziektebeloop na 1 jaar en het langere termijn beloop na 3 en 5 jaar bij RA kunnen voorspellen. Naast deze studies werd in twee aanvullende prospectieve studies de bijdrage van predictoren bestudeerd die in de psychologische literatuur tot nu toe weinig aandacht hebben gekregen: generieke ziektecognities en fysiologische pijnreactiviteit. De resultaten van deze studies worden hieronder samengevat.

Coping en Sociale Steun

Predictie van ziekteactiviteit. Er is een relatief lange onderzoekstraditie naar de invloed van psychologische factoren, vooral stressvolle gebeurtenissen, op ziekteactiviteit bij de autoimmuun ziekte RA door de veronderstelde relatie tussen stress en het immuunsysteem. Op basis van stress-vulnerabiliteit modellen werd in de huidige studie de rol van verschillende stressoren (major life events en ziekte-gerelateerde stressoren) en vulnerabiliteitsfactoren (de persoonlijkheidskenmerken neuroticisme en extraversie, stress coping en sociale steun) onderzocht bij 78 recent gediagnosticeerde RA patiënten voor het beloop van ziekteactiviteit 1, 3 en 5 jaar na de diagnose *(hoofdstuk 3.1.1).* Geen van de stress-vulnerabiliteit factoren voorspelde het beloop van ziekteactiviteit na 1 jaar. Dit werd toegeschreven aan het effect van de medicatie, zoals bleek uit een sterke daling van de ziekteactiviteit in het eerste jaar na de diagnose. Op de langere termijn, na 3 en 5 jaar bleek een passief-vermijdende manier van stress coping een ongunstiger beloop van ziekteactiviteit te voorspellen. Ook voorspelde een laag niveau van sociale steun een ongunstiger beloop van ziekteactiviteit 3 jaar na de diagnose. In overeenstemming met eerdere bevindingen bij patiënten met langdurige RA wijzen de resultaten erop dat passieve stress coping en een laag niveau van sociale steun mogelijke risicofactoren zijn voor een ongunstig langere termijn beloop van ziekteactiviteit bij RA patiënten.

Predictie van functionele beperkingen en pijn. Fear-avoidance modellen veronderstellen dat vermijdingsfactoren, zoals het vermijden van activiteiten en catastroferende gedachten over pijn, en een laag niveau van sociale steun het beloop van functionele bewegingsbeperkingen en pijn kunnen beïnvloeden. In twee studies werd de rol van cognitief-gedragsmatige vermijdingsfactoren

(passieve pijn-coping) en sociale steun ten tijde van de diagnose onderzocht voor het beloop van functionele beperkingen en pijn bij 91 RA patiënten 1 jaar na de diagnose en bij 78 RA patiënten van wie follow-up gegevens beschikbaar waren na 3 en 5 jaar *(hoofdstukken 3.1.2.1 - 3.1.2.2).* Uit de resultaten bleek dat een passieve manier van coping met pijn (vermijden van activiteiten en catastroferende gedachten over pijn) een ongunstiger beloop van functionele beperkingen 1 en 3 jaar na de diagnose voorspelden. Ook voorspelde een laag niveau van sociale steun een ongunstiger beloop van functionele bewegingsbeperkingen 1, 3 en 5 jaar na de diagnose. Minder sociale steun bleek tevens een ongunstiger beloop van pijn na 3 en 5 jaar te voorspellen. In overeenstemming met fear-avoidance modellen laten deze resultaten zien dat cognitieve en gedragsmatige vermijdingsfactoren in het omgaan met pijn en een laag niveau van sociale steun een relatief langdurige invloed kunnen hebben op het lichamelijk functioneren bij RA patiënten.

Predictie van psychische distress. Stress-vulnerabiliteit modellen beogen te verklaren welke factoren ervoor verantwoordelijk zijn dat patiënten met een chronische aandoening een verhoogde mate van psychische distress ontwikkelen. In twee studies werd de relatieve bijdrage van verschillende stressoren (major life events en ziekte-gerelateerde stressoren) en vulnerabiliteitsfactoren (de persoonlijkheidskenmerken neuroticisme en extraversie, stress coping en sociale steun) onderzocht voor het beloop van het psychisch functioneren (angst en depressieve stemming) na 1 jaar bij 91 RA patiënten en na 3 en 5 jaar bij 78 RA patiënten van wie follow-up gegevens aanwezig waren *(hoofdstukken 3.1.3.1 - 3.1.3.2).* In overeenstemming met bevindingen bij langdurige RA bleek dat bij ca. 30% van de patiënten met vroege RA sprake is van een verhoogde mate van psychische distress, vergelijkbaar met subklinische niveaus van angst en depressie. Uit de predictie bleek dat een laag niveau van sociale steun een ongunstiger beloop van depressieve stemming in het eerste jaar na de diagnose voorspelde. Op de langere termijn, 3 en 5 jaar na de diagnose, voorspelde vooral het persoonlijkheidskenmerk neuroticisme een ongunstiger beloop van angst en depressieve stemming. In overeenstemming met resultaten in de algemene bevolking en bij langdurige RA patiënten wijzen deze resultaten op de rol van neuroticisme als risicofactor voor het psychisch functioneren van RA patiënten op de langere termijn.

Ziektecognities

In de psychologische literatuur over chronische aandoeningen wordt verondersteld dat ziektecognities een belangrijke rol spelen voor het ziektebeloop. Ondanks verschillen in conceptualisering blijkt uit onderzoek dat specifieke, controle-gerelateerde cognities, zoals waargenomen hulpeloosheid ten aanzien van de ziekte, het ziektebeloop bij een groot aantal chronisch zieken, inclusief RA patiënten, ongunstig beïnvloeden. Tot nu toe zijn er echter geen instrumenten beschikbaar waarmee ziektecognities van hulpeloosheid bij verschillende groepen

chronisch zieken kunnen worden vergeleken. Ook is er nauwelijks iets bekend over adaptieve ziektecognities, dat wil zeggen, cognities die een gunstige invloed hebben op het ziektebeloop van chronisch zieken. Hoewel bijvoorbeeld een hoge mate van waargenomen controle verondersteld wordt een gunstige invloed te hebben, werd dit bij chronisch zieken niet altijd bevestigd. Een hoge mate van waargenomen controle bleek bij RA patiënten en andere chronisch zieken het ziektebeloop juist ongunstig te kunnen beïnvloeden, bijvoorbeeld in fasen wanneer de ziekte actief en oncontroleerbaar is. Op grond van deze gegevens werd verondersteld dat adaptieve ziektecognities bij chronisch zieken vooral gericht moeten zijn op een (her)evaluatie van de negatieve betekenis van de ziekte in plaats van op waargenomen controle.

Op basis van de literatuur werd vervolgens een vragenlijst ontwikkeld om de volgende generieke ziektecognities bij chronisch zieken in kaart te brengen: 'hulpeloosheid' waardoor de negatieve betekenis van de ziekte wordt versterkt, 'acceptatie' waardoor de negatieve betekenis van de ziekte wordt verminderd, en 'perceived benefits' waardoor een positieve betekenis aan de ziekte wordt toegevoegd door ook positieve lange-termijn gevolgen van de ziekte te zien *(hoofdstuk 3.2)*. De betrouwbaarheid en validiteit van deze vragenlijst, de Ziekte Cognitie Lijst (ZCL), werd bij 263 RA patiënten en 167 patiënten met multiple sclerosis (MS) onderzocht. Uit de resultaten bleek dat de ZCL de verschillende ziektecognities van hulpeloosheid, acceptatie en perceived benefits betrouwbaar en valide in kaart brengt. Ook werd een hoge mate van overeenstemming gevonden tussen beide groepen chronisch zieken in de structuur van de vragenlijst en de concurrente en predictieve validiteit. Tevens bleken de ziektecognities alle dimensies van het ziektebeloop na 1 jaar te voorspellen (ziekteactiviteit, lichamelijk en psychisch functioneren), waarbij hulpeloosheid consistent negatief, en acceptatie en perceived benefits consistent positief gerelateerd waren aan een gunstiger ziektebeloop na 1 jaar bij patiënten met RA en MS. Er werd geconcludeerd dat de ZCL een betrouwbare en valide vragenlijst is om generieke, maladaptieve en adaptieve ziektecognities bij verschillende groepen chronisch zieken vast te stellen.

Fysiologische Pijnreactiviteit

Fear-avoidance modellen veronderstellen dat niet alleen cognitieve en gedragsmatige reacties op pijn, maar ook fysiologische reacties op pijn het lichamelijk functioneren bij chronische pijn patiënten kunnen beïnvloeden. Met name autonome en musculaire reacties op pijn worden verondersteld een ongunstige invloed te hebben op het beloop van pijn. Empirische ondersteuning voor pijngerelateerde fysiologische reacties werd gevonden in experimenteel onderzoek bij RA en andere groepen chronische pijn patiënten. Ook bleek in cross-sectioneel onderzoek bij een heterogene groep chronische pijn patiënten een hogere, zelfgerapporteerde fysiologische pijnreactiviteit gepaard te gaan met een

hogere mate van pijn. Er is echter weinig bekend over de directe invloed van fysiologische pijnreactiviteit op pijn of andere indicatoren van het lichamelijk functioneren bij chronische pijn patiënten. In de huidige studie *(hoofdstuk 3.3)* werd de bijdrage van zelfgerapporteerde fysiologische pijnreactiviteit vergeleken met die van cognitief-gedragsmatige vermijdingsfactoren (passieve coping met pijn) voor het beloop van pijn na 1 jaar bij 95 RA patiënten. Uit de resultaten bleek dat alleen de fysiologische pijnreactiviteit een ongunstig beloop van pijn voorspelde. Tevens bleek in Structural Equation Modeling dat neuroticisme verband hield met een hogere fysiologische pijnreactiviteit die op zijn beurt weer de enige voorspeller was voor een ongunstig pijnbeloop. Er werd geconcludeerd dat fysiologische pijnreactiviteit een betere voorspeller voor het beloop van pijn bij RA patiënten is dan de cognitieve en gedragsmatige reacties op pijn. Uit de analyses van de zelfgerapporteerde, autonome en musculaire reacties bij RA patiënten bleek tevens dat hun fysiologische reacties niet overeenkomen met gegevens uit ander onderzoek bij heterogene groepen chronische pijn patiënten. Dit gegeven wijst mogelijk op een specifiek patroon van fysiologische pijnreactiviteit bij RA patiënten.

MODIFICATIE VAN HET ZIEKTEBELOOP: TAILOR-MADE BEHANDELING BIJ RA

In eerder onderzoek naar psychologische interventies bij RA werd vooral de effectiviteit van gestandaardiseerde groepsprogramma's onderzocht die voor alle patiënten open staan. De interventies kunnen worden ingedeeld in drie categorieën die verschillen in de mate waarin ze veranderingen in gedragsfactoren beogen: patiënteneducatie, zelfredzaamheidtrainingen en cognitieve gedragstherapie. Hoewel in sommige studies positieve effecten van psychologische behandelingen werden gevonden, vooral voor cognitieve gedragstherapie, blijkt uit recent uitgevoerde meta-analyses dat de effecten klein en van korte duur zijn. In de psychologische literatuur over RA en andere chronische pijn aandoeningen wordt gesuggereerd dat tailor-made behandelingen, zoals bijvoorbeeld een individueel afgestemde behandeling voor geselecteerde patiënten in een bepaalde fase van de ziekte, de effectiviteit mogelijk kan vergroten. Op grond van de bevindingen van de prospectieve studies in dit proefschrift werd verondersteld dat psychologische interventies voor RA patiënten effectiever zijn indien deze individueel afgestemd worden op patiënten met een psychologisch risicoprofiel in een relatief vroege fase van RA.

In een gerandomiseerde en gecontroleerde studie werd de effectiviteit geëvalueerd van een tailor-made behandeling bij 64 RA patiënten met een relatief korte ziekteduur en een psychologisch risicoprofiel *(hoofdstuk 4)*. Alle patiënten ontvingen de reguliere zorg van de reumatoloog en de reumaconsulent. De helft

van de patiënten ontving tevens op individuele basis, kortdurende cognitieve gedragstherapie die bestond uit twee van de vier mogelijke behandelmodules. De keuze van de behandelmodules was gebaseerd op de voorkeur van de patiënten. Dit resulteerde in de meest frequente toepassing van de module voor vermoeidheid, gevolgd door de modules voor negatieve stemming, sociale relaties en tenslotte pijn/functionele beperkingen. De behandeling bleek een gunstig effect te hebben op het lichamelijk, psychisch en sociaal functioneren. In vergelijking met de controleconditie hadden patiënten uit de behandelconditie minder last van vermoeidheid en depressiviteit, zowel direct na afloop van de behandeling als ook bij de follow-up meting, 6 maanden later, en ervoeren patiënten meer steun vanuit hun omgeving bij de follow-up meting. Ook rapporteerden patiënten minder hulpeloosheid ten aanzien van RA direct na afloop van de behandeling en bij de follow-up meting, een meer actieve manier van omgaan met stress in het dagelijks leven na afloop van de behandeling en een toegenomen therapietrouw ten aanzien van de voorgeschreven medicatie bij de follow-up meting in vergelijking met patiënten uit de controleconditie. De effecten bleken zowel bij de nameting als ook bij de follow-up meting gemiddeld van een modale grootte te zijn (effectgrootte tussen .48 en .55 voor het lichamelijk en psychisch functioneren). Ook kenmerkte zich de behandeling door een relatief laag percentage uitvallers (6% in de behandelconditie). Er werd geconcludeerd dat, in vergelijking met gegevens uit recent verschenen meta-analyses, tailor-made behandeling bij RA patiënten een veelbelovende manier is om de effectiviteit van psychologische interventies te vergroten.

CONCLUSIES EN KLINISCHE IMPLICATIES

De belangrijkste conclusies en klinische implicaties van het onderzoek kunnen als volgt worden samengevat:

1. Ziektecognities, coping met stress en pijn en sociale steun beïnvloeden het ziektebeloop bij RA en kunnen als psychologische risicofactoren worden beschouwd.
2. Psychologische risicofactoren zijn reeds bij de diagnose manifest en beïnvloeden het ziektebeloop bij RA op de langere termijn.
3. Kennis over psychologische risicofactoren maakt het mogelijk om RA patiënten met een psychologisch risicoprofiel reeds in een vroeg stadium van de ziekte op te sporen.
4. Een tailor-made behandeling, dat wil zeggen een op de patiënt afgestemde behandeling voor patiënten met een psychologisch risicoprofiel in een vroege fase van de ziekte, is een veelbelovende manier om de effectiviteit van psychologische interventies bij RA te vergroten.

Toekomstig onderzoek dient zich vooral te richten op de onderliggende mechanismen van de psychologische risicofactoren en de ontwikkeling van daarop afgestemde behandelingen voor patiënten at risk.

Dankwoord

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Te beginnen bij de patiënten met reumatoïde artritis en multiple sclerosis, degenen waar patiëntengebonden onderzoek tenslotte om draait. Meer dan 1000 patiënten hebben deel uitgemaakt van de verschillende studies in dit proefschrift. Ze hebben vaak meerdere keren de tijd genomen voor extra bezoeken op de polikliniek voor het lichamelijk onderzoek en het invullen van de vragenlijstboekjes. Alleen door de trouwe deelname van velen werden de studies in dit proefschrift mogelijk gemaakt.

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Andrea

Curriculum Vitae

Andrea Walburga Maria Evers was born on February 7, 1967, in Arnsberg, Germany. After graduating in 1986 from the Mariengymnasium high school in Arnsberg, she started to study psychology at the University of Bielefeld, Germany. From 1988 to 1992, she also worked as a student research assistant at the University of Bielefeld. In 1992, she received a one-year grant for science and technology studies in the Social and Behavioral Sciences at the University of Amsterdam. She subsequently completed her graduation research project in the Department of Clinical Psychology at the University of Amsterdam, for which she received the 1994 graduation award from the Faculty of Psychology. From 1990 to 1994, she also completed a basic program in client-centered psychotherapy at the German Society for Scientific Client-Centered Therapy and in behavior therapy at the German Society for Behavior Therapy. After graduating in 1994 with a degree in clinical psychology (i.e. methods of behavior change), she worked several months as a researcher in the Department of Clinical Psychology at the University of Amsterdam. Then in 1995, she started working as a psychologist/researcher in the Department of Medical Psychology at the University Medical Center St Radboud in Nijmegen. Part of her work here included the present Ph.D. thesis, supported by grants from the Dutch Arthritis Association and incooperated in the Experimental Psychopathology Research School program. In 1997, she also started the psychotherapist and behavior therapist program at the Dutch Society for Cognitive-Behavior Therapy (VGCT). She has been a registered health care psychologist since 2000 and will soon be a registered psychotherapist and behavior therapist. Currently, she is working as an assistant professor and health care psychologist in the Department of Medical Psychology at the University Medical Center St Radboud in Nijmegen, where her clinical and research activities focus on the role of cognitive-behavioral factors in chronic conditions.

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Abbreviations

ACR	American College of Rheumatology
AIMS	Arthritis Impact Measurement Scales
BDI	Beck Depression Questionnaire
CBT	Cognitive-Behavioral Therapy
CC	Control Conditon
CFI	Comparative Fit Index
CIS	Checklist Individual Strength
CRP	C-Reactive Protein
DAS	Disease Activity Score
DMARD	Disease-Modifying Anti-Rheumatic Drug
EPQ	Eysenck Personality Questionnaire
ESR	Erythrocyte Sedimentation Rate
HAQ	Health Assessment Questionnaire
ICQ	Illness Cognition Questionnaire
IFI	Incremental Goodness-of-Fit Index
IRGL	Impact of Rheumatic Diseases on General Health and Lifestyle
LES	Life Experience Survey
LOT	Life Orientation Test
M	Mean
MS	Multiple Sclerosis
NS	Nonsignificant
NSAID	Non-Steroidal Anti-Inflammatory Drug
OA	Osteoarthritis
PCI	Pain Coping Inventory
RA	Rheumatoid Arthritis
SD	Standard Deviation
SIP	Sickness Impact Profile
STAI	State-Trait Anxiety Inventory
TLI	Tucker-Lewis Index
UCL	Utrecht Coping List
VAS	Visual Analogue Scale