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ORIGINAL ARTICLE

Impact of Psychological Factors on Subjective Disease Activity Assessments in Patients With Severe Rheumatoid Arthritis

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Objective. **The Disease Activity Score in 28 joints (DAS28), used to assess disease activity in rheumatoid arthritis (RA), is a composite score comprising clinical, biochemical, and patient self-report measures. We hypothesized that psychological factors (cognitions and mood) would be more strongly associated with patient-reported components of the DAS28 than clinical or biochemical components.**

Methods. **A cross-sectional, observational study of 322 RA patients with active disease (mean DAS28 6.0) awaiting therapy with a biologic agent was undertaken. Patients' illness beliefs, treatment beliefs, and mood were measured using the Brief Illness Perception Questionnaire (IPQ), the Beliefs about Medicines Questionnaire (BMQ), and the Hospital Anxiety and Depression Scale (HADS), respectively. Relationships between psychological factors and 1) total DAS28 and 2) individual components of the DAS28 were analyzed using linear regression.**

Results. **Total DAS28 produced significant but weak associations with 2 of the Brief IPQ items, but no associations with BMQ or HADS scores. There were larger significant associations between the patient-reported visual analog scale (VAS) with 5 items of the Brief IPQ and with HADS depression. Low illness coherence was associated with higher tender joint count. Three Brief IPQ items and HADS anxiety scores were significantly associated with C-reactive protein level or erythrocyte sedimentation rate. No psychological factors were associated with the swollen joint count.**

Conclusion. **One of the subjective components of the DAS28, patient VAS, was highly correlated with cognitive factors and depression in those with severe RA. By reporting individual DAS28 components, clinicians may be better able to assess the impact of therapies on each component, adjusting approaches according to patients' needs.**

INTRODUCTION

Severity of rheumatoid arthritis (RA) is assessed using the Disease Activity Score in 28 joints (DAS28). The DAS28 is a composite score comprising clinician report of signs, patient self-report, and biochemical measures. It was developed originally to enable the monitoring of RA activity and is the standard measure used to gauge response to therapy. Recently, the DAS28 has emerged as a main criterion for determining treatment pathways, in particular decisions about stepping up from traditional disease-

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Significance & Innovations

- The Disease Activity Score in 28 joints (DAS28) has emerged as a main criterion for determining rheumatoid arthritis (RA) treatment pathways, including decisions about use of therapy with biologic agents.
- In patients with severe disease awaiting initiation of therapy with a biologic agent, the patient visual analog scale component of the DAS28 was strongly associated with beliefs about RA and depression.
- High levels of depression and anxiety were recorded, indicating that routine screening may be appropriate for people awaiting therapy with a biologic agent.
- This is the first study of its kind in patients with high levels of active disease and indicates that clinicians may benefit from reporting individual DAS28 component scores separately alongside total DAS28.

modifying antirheumatic drugs to use of therapy with biologic agents. The DAS28 combines scores for 3 main areas: swollen joint count (SJC) and tender joint count (TJC), a biologic marker of inflammation (erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP] level), and a visual analog scale (VAS) score of global well-being (1).

The patient-reported component or VAS can account for more than one-quarter of the overall DAS28 score necessary to make an individual eligible for treatment with a biologic agent. As an aggregate score, the DAS28 has emerged as a core treatment outcome measure; however, the performance of individual components of the DAS28 has not been well explored.

Evidence from other inflammatory conditions suggests different aspects of the condition may be more responsive to different treatments (2). For example, high TJC in the absence of objective joint swelling in RA may suggest that pain management strategies should be considered. It has become increasingly evident that the ways in which patients perceive their RA have a strong influence upon disease outcome (3,4). Individuals' beliefs about the nature of their condition (illness perceptions) form a key part of Leventhal's Self-Regulatory Model (or the Common-Sense Model), which provides a framework for understanding the impact that illness beliefs and emotions have on how an individual copes, adapts, and responds to illness (5,6). The model can be represented as a 3-stage process in which a patient's perception of their illness (stage 1) guides a coping or an action-planning response (stage 2) followed by the appraisal stage (stage 3), whereby the individual monitors the success or failure of the coping process (6,7) (Figure 1). Leventhal et al identified 5 key dimensions of illness beliefs that are central to this model (8). These include identity (beliefs about the nature of the illness), consequences (the personal impact of the illness on mental, physical, and social functioning), cause, controllability of the symptoms, and timeline (perception of the course of the disease determined by whether symptoms are acute, chronic, or cyclical in nature). Interestingly, a study of 121 patients with RA found that illness perceptions explained a substantial portion (35%) of the variance in disease-specific physical functioning, with clinical factors accounting for only 6% of the variance (9). This and findings from other studies indicate that individuals who perceive their symptoms as less controllable adapt less well to living with RA (10–13). Beliefs in significant negative consequences and a chronic timeline of disease duration are other dimensions that have been reported to be associated with a number of outcomes in RA, including greater disability (12), pain (10), and low mood (14).

Anxiety and depression are common among patients with RA, with the prevalence being higher than that of the general population (28–44% versus 6.6%) (15–18). Studies have shown that those who perceive their RA as having serious negative consequences experience high states of anxiety, whereas those who have more symptoms (identity construct) experience more severe depression (12,19).

We hypothesized that patients' beliefs and mood are differentially associated with subjective (VAS, TJC) and objective (ESR/CRP, SJC) components of the DAS28. Our aim was to explore the relationships between illness beliefs, treatment beliefs, and mood with separate indicators of disease activity in patients with severe and active RA. Since mood may be influenced by illness perception, a secondary aim was to explore the relationship between the 2 factors.

PATIENTS AND METHODS

Study design. The current study utilized baseline (cross-sectional) data from a larger multicenter, prospective, observational study of RA patients about to be started on an anti–tumor necrosis factor (anti-TNF) agent, involving 54 centers from around the UK.

Study participants. Between November 2008 and January 2011, patients were recruited into the study from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate, which was established to study predictors of treatment response to biologic drugs (for a list of members, see Supplementary Appendix A, available in the online version of this article at http://onlinelibrary.wiley.com/doi/10.1002/acr.22249/abstract). Consenting participants were eligible to take part in the study if they had a diagnosis of RA as defined by the American College of Rheumatology 1987 criteria (20) and were about to commence anti-TNF therapy (adalimumab, infliximab, certolizumab, golimumab, or etanercept). Ethical approval was obtained from the North West Ethics Research Committee (COREC 04/Q1403/37).

Questionnaire collection. Individuals attending outpatient clinics and about to commence anti-TNF drugs completed validated questionnaires assessing illness beliefs (the Brief Illness Perception Questionnaire [IPQ]) (21), beliefs about medicines (the Beliefs about Medicines Questionnaire [BMQ]) (22), and mood (the Hospital Anxiety and Depression Scale [HADS]) (23). Demographic and

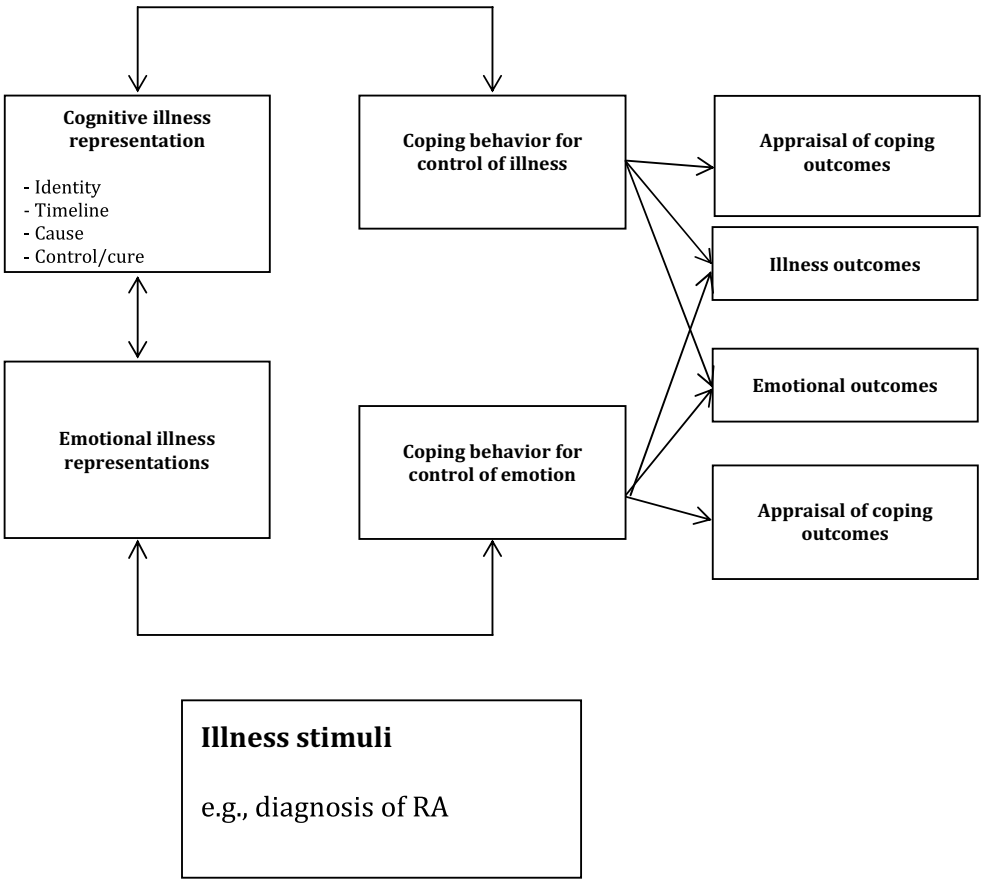

Figure 1. Leventhal's Self-Regulatory Model of illness perceptions. Patients' beliefs about their illness comprise 5 key domains (identity, timeline, cause, control/cure, and consequences), used to aid understanding of illness and guide a coping response. Patients will then appraise the process to determine the success or failure of the coping strategy. RA = rheumatoid arthritis. Adapted, with permission, from Hagger MS, Orbell S. A meta-analytic review of the common-sense model of illness representations. Psychol Health 2003;18:141–84.

clinical assessments, including the DAS28, were collected at the same time point.

Brief IPQ. Illness perceptions were assessed using the Brief IPQ, a 9-item questionnaire used to assess patients' cognitive and emotional perceptions of disease. Each item corresponding to a particular domain of illness perception is scored using a 10-point rating scale, where item 1 = consequences, item 2 = timeline, item 3 = personal control, item 4 = treatment control, item 5 = identity, item 6 = coherence, item 7 = emotional representation, item 8 = concern, and item 9 = cause. Each item stands alone, with higher scores reflecting a more threatening view of illness.

HADS. The HADS is a 14-item questionnaire used to assess levels of anxiety (7 items) and depression (7 items). It was designed specifically for use with individuals from within physical disease populations, since it excludes somatic components of depression (e.g., appetite loss) that may be confounded by physical disease symptoms related to the illness. Each question has a 4-point Likert scale and is scored between 0 and 3, e.g., "I can sit at ease and feel relaxed," with responses of 0 = definitely, 1 = usually, 2 = not often, and 3 = not at all. Anxiety and depression are scored separately using the 7-item subscales. Higher scores indicate a more severe mood disorder. Scores are interpreted as follows: normal = 0–7, mild = 8–10, moderate = 11–15, and severe = 16–21.

BMQ. Patients' beliefs about the necessity of their prescribed medication and concerns related to taking the medication were evaluated using the BMQ, a 10-item validated measure of treatment beliefs. The BMQ consists of two 5-item subscales assessing 2 domains: perceived concerns about and perceived necessity of their prescribed medication. Items are presented in a mixed order and scored on a 5-point Likert scale (range 1–5, where 1 = strongly disagree and 5 = strongly agree). Higher scores represent stronger perceived concerns and stronger perceived necessity beliefs for the prescribed drug. The BMQ has been used in studies of many conditions, including RA (24).

DAS28. The DAS28 was calculated using established methods (online at http://www.das-score.nl/).

Statistical analyses. All questionnaires were scored using scripts created in Stata (2005). DAS28 scores, supplemented with CRP data, were also used where DAS28-ESR scores were not available. Clinical data were combined with questionnaire data using the study identification number unique to each patient.

All statistical analyses were performed using Stata. Paired *t*-tests and chi-square tests were used to analyze parametric and nonparametric data, respectively. Robust linear regression analyses were used to assess direct relationships between the study variables (illness perceptions, medication beliefs, and anxiety and depression) and DAS28 scores (outcome measure). Similar analyses were performed using the individual components of the DAS28 as outcome variables (patient VAS, TJC, SJC, and ESR and CRP level). The relationships between anxiety and depression with illness perceptions were investigated using linear regression. To illustrate the strength of the relationships between domains of the Brief IPQ, the BMQ, and the HADS scores with both composite and individual DAS28 components, Spearman's correlation coefficients were calculated and are reported alongside the regression data. All reported *P* values are 2-tailed and the threshold for statistical significance was set at 5%.

RESULTS

Patient characteristics. In total, 518 patients were recruited to the study in the specified time period. Complete baseline data were returned by 322 individuals (62% of the total). Clinical and demographic information for individuals who did and did not return their questionnaires is shown in Table 1. Individuals recruited into the study had longstanding disease (median 7.6 years, interquartile range 2.7–16.1 years), and the high DAS28 scores (mean ± SD 6.00 ± 0.92) were indicative of the expected levels of severe disease in participants about to commence anti-TNF therapy. There were no significant differences between those who did and did not return the questionnaire.

Summary statistics. Descriptive statistics for each of the questionnaire domains are shown in Table 2. Levels of missing data were very low (i.e., 1.8%, 1.8%, 2.5%, and 3.4% for the Brief IPQ, HADS, BMQ necessity, and BMQ concerns, respectively).

Table 1. Baseline clinical and demographic data for study participants who did and did not return questionnaires*

Cohort characteristics	Returned questionnaires (n = 322)	Nonreturned questionnaires (n = 196)	*P*
Age, mean ± SD years	55.8 ± 12.5	55.6 ± 12.8	0.82
Women, no. (%)	235 (73.0)	144 (77.8)	0.23
Disease duration, median (IQR) years	7.6 (2.7–16.1)	8.3 (3.8–16.3)	0.45
DAS28, mean ± SD	6.00 ± 0.92	6.02 ± 0.92	0.92
HAQ score, mean ± SD	1.69 ± 0.60	1.64 ± 0.79	0.83
Concurrent DMARDs, no. (%)	273 (85.9)	159 (87.4)	0.64
Previous biologic agent, no. (%)	22 (6.8)	17 (8.7)	0.12

* IQR = interquartile range; DAS28 = Disease Activity Score in 28 joints; HAQ = Health Assessment Questionnaire; DMARDs = disease-modifying antirheumatic drugs.

Table 2. Descriptive statistics for the Brief IPQ and BMQ domains and the HADS*

Questionnaire	Median (IQR)	N
Brief IPQ (possible range 0–10)		
Consequences	8 (7–8)	315
Timeline	10 (9–10)	312
Personal control	6 (4–8)	316
Treatment control	2 (1–4)	312
Identity	8 (7–9)	316
Concern	8 (7–10)	316
Coherence	2 (1–3.5)	316
Emotional representation	7 (5–8)	313
BMQ		
Concern	16 (13–18)	311
Necessity	21 (19–23)	314
HADS		
Anxiety	8 (5–11)	316
Depression	7 (5–10)	316

* IPQ = Illness Perception Questionnaire; BMQ = Beliefs about Medicines Questionnaire; HADS = Hospital Anxiety and Depression Scale; IQR = interquartile range.

Brief IPQ scores indicated that RA has a substantial impact upon patients' lives (consequences), with the majority experiencing severe symptoms (identity). Patients reported a high level of concern about their RA and high scores on the item assessing emotional representations. Treatment control scores were noticeably low, indicating that patients did not believe that medicine could help them control their RA, yet BMQ necessity scores were high, suggesting that patients believed they need the medication. Patients indicated poor understanding of their disease (coherence), and approximately half of the patients reported anxiety and depression levels above the levels considered borderline (HADS anxiety: 51.1% scored >7 and 26.5% scored >11; HADS depression: 47.3% scored >7 and 20.6% scored >11). Levels of depression for this sample were higher than those previously reported in an RA population (17,25,26).

Relationship with composite DAS28. Results for the linear regression between total DAS28 and baseline demographic factors are shown in Table 3. Disability at baseline, as measured by the baseline Health Assessment Questionnaire score, demonstrated a statistically significant association with total DAS28 ($\beta = 0.34$, $P < 0.0001$).

Table 3. Association of baseline variables and baseline Disease Activity Score in 28 joints scores*

Covariate	Standardized β	*P*
Sex	0.02	0.85
Age at baseline	0.0002	0.97
Disease duration	−0.01	0.08
Current smoker	−0.03	0.83
Systemic steroids (NSAIDs)	0.07	0.36
Baseline HAQ score	0.34	< 0.0001

* NSAIDs = nonsteroidal antiinflammatory drugs; HAQ = Health Assessment Questionnaire.

Table 4. Linear regression analyses and Spearman's correlations between the Brief Illness Perception Questionnaire domains and the composite Disease Activity Score in 28 joints*

Question	β (95% CI)	Spearman's ρ	Correlation P
Consequence	0.08 (0.02, 0.15)	0.14	0.01
Timeline	0.04 (−0.03, 0.11)	0.07	0.23
Personal control	0.01 (−0.03, 0.05)	0.07	0.19
Treatment control	0.001 (−0.06, 0.06)	0.01	0.80
Identity	0.16 (0.09, 0.23)	0.27	< 0.001
Concern	0.05 (0.005, 0.10)	0.14	0.01
Coherence	−0.01 (−0.05, 0.04)	−0.05	0.39
Emotional representation	0.02 (−0.02, 0.06)	0.09	0.12

* 95% CI = 95% confidence interval.

There were no statistically significant associations of total DAS28 with anxiety, depression, and the concerns domain of the BMQ. Total DAS28 showed a significant (weak) positive correlation with the Brief IPQ dimension of illness consequences ($\beta = 0.08$ [95% confidence interval (95% CI) 0.02, 0.15], $P = 0.01$), and a stronger correlation with the construct of illness identity ($\beta = 0.16$ [95% CI 0.09, 0.23], $P < 0.001$) (Table 4). When incorporated into a model adjusting for other Brief IPQ variables, only the identity domain, which asks patients about the severity and number of symptoms they experience associated with RA, was significantly associated with total DAS28 ($P < 0.001$).

Relationship with individual DAS28 components. Analyses were undertaken using the individual components of the DAS28 score (Table 5).

Patient VAS. Depression was significantly associated with patient VAS ($\beta = 0.90$ [95% CI 0.40, 1.40], $P < 0.001$); however, this was not the case for anxiety ($\beta = 0.48$ [95% CI −0.012, 0.95], $P = 0.11$). The Brief IPQ dimensions of illness consequence, personal control, concern, identity, and emotional representation were each positively correlated with patient VAS.

TJC. One domain of the Brief IPQ was very highly correlated with the TJC28: the illness coherence domain ($\beta = -0.61$ [95% CI −0.95, −0.28], $P = 0.0003$). There were no significant associations with the other cognitive measures, including beliefs about medicines, and neither of the associations between the mood measures (anxiety and depression) and the TJC was significant.

SJC. None of the belief or mood measures was associated with the SJC.

ESR or CRP level. The Brief IPQ illness identity measure correlated strongly with ESR and CRP level ($\beta = 2.19$ [95% CI 0.53, 3.85], $P = 0.002$ and $\beta = 2.11$ [95% CI 0.48, 4.69], $P = 0.004$, respectively), as did the illness coherence score ($\beta = 1.60$ [95% CI 0.54, 2.67], $P = 0.03$ and $\beta = 1.39$ [95% CI 0.16, 2.95], $P = 0.04$, respectively). The consequences domain was significantly correlated with CRP level ($\beta = 1.74$ [95% CI −0.71, 4.19], $P = 0.04$). The concerns domain of the BMQ was not significantly associated with any of the individual DAS28 components (Table 5).

Relationships between mood (anxiety and depression) and Brief IPQ. Levels of anxiety and depression were relatively high in this sample (Table 2). Both anxiety and depression correlated significantly with most of the Brief IPQ dimensions (Table 6). There were strong associations with illness consequences and illness identity. These results are of particular interest because anxiety and depression were not significantly associated with total DAS28 in the initial analyses. This indicates that illness perceptions are associated with mood in patients with severe disease.

As would be anticipated, illness concerns and emotional representation are strongly associated with the 2 mood measures (Table 6). The treatment concerns domain was associated with both anxiety and depression. Adjusting for age and sex in all of the analyses did not alter the findings.

DISCUSSION

The results of the present study partially support the hypothesis that psychological factors associate differentially with subjective and objective components of the total DAS28 in patients with severe RA. There were particularly strong correlations between depression and illness cognitions with one of the subjective components of DAS28, specifically patient VAS score.

This work highlights an important clinical message that may seem obvious but that has not previously been reported, i.e., clinicians should interpret DAS28 values in the context of the contributions of the individual scores, some of which may be more or less influenced by the individual's response to a biologic agent–based therapy. In addition and in particular, high VAS scores (which could significantly elevate a DAS28 score) may be more strongly influenced by other factors such as psychological variables.

The finding that psychological factors have a different relationship with some components of the DAS28 suggests that routine assessment of mood and beliefs, plus separate reporting of the individual components of the DAS28, would be useful in guiding patient management, particularly in situations where improvements over time or with new treatments occurred in some components and not in others. Given the importance of the DAS28 as a criterion for treatment decision making as well as its role as the main measure of treatment outcome, an improved under-

Table 5. Robust regression analyses and Spearman's correlations between Brief IPQ and BMQ dimensions, HADS anxiety, and HADS depression with individual components of the Disease Activity Score in 28 joints (patient VAS, TJC, SJC, ESR, and CRP level)*

	Patient VAS			TJC28			SJC28			ESR			CRP level		
	β (95% CI)	Spearman's ρ	Correlation P	β (95% CI)	Spearman's ρ	Correlation P	β (95% CI)	Spearman's ρ	Correlation P	β (95% CI)	Spearman's ρ	Correlation P	β (95% CI)	Spearman's ρ	Correlation P
Brief IPQ item															
Consequence	2.86 (1.63, 4.10)	0.27	< 0.0001	0.50 (0.003, 1.00)	0.10	0.09	−0.03 (−0.45, 0.40)	−0.02	0.68	0.60 (−0.94, 2.13)	0.04	0.56	1.74 (−0.71, 4.19)	0.15	0.04
Timeline	0.52 (−0.95, 1.98)	0.008	0.89	0.39 (−0.18, 0.95)	0.06	0.32	0.03 (−0.45, 0.52)	−0.03	0.59	0.85 (−1.04, 2.75)	0.03	0.64	0.34 (−2.14, 2.82)	0.04	0.63
Personal control	1.04 (0.25, 1.84)	0.16	0.006	−0.004 (−0.32, 0.31)	0.005	0.94	−0.10 (−0.37, 0.17)	−0.03	0.62	−0.29 (−1.28, 0.70)	−0.02	0.73	0.80 (−0.69, 2.29)	0.10	0.18
Treatment control	−1.10 (−2.37, 0.17)	−0.10	0.10	0.16 (−0.31, 0.63)	0.04	0.49	0.09 (−0.31, 0.50)	0.03	0.65	0.48 (−0.99, 1.95)	0.02	0.74	0.18 (−1.98, 2.34)	0.03	0.70
Identity	3.41 (2.03, 4.78)	0.29	< 0.001	0.66 (0.11, 1.21)	0.10	0.07	−0.17 (−0.65, 0.30)	−0.04	0.47	2.19 (0.53, 3.85)	0.19	0.002	2.11 (0.48, 4.69)	0.22	0.004
Concern	2.06 (1.05, 3.06)	0.23	0.0001	0.22 (−0.17, 0.61)	0.06	0.26	−0.002 (−0.34, 0.33)	−0.01	0.87	0.44 (−0.79, 1.67)	0.06	0.31	0.22 (−1.68, 2.12)	0.03	0.73
Coherence	−0.35 (−1.23, 0.54)	−0.03	0.58	−0.61 (−0.95, −0.28)	−0.21	0.0003	0.05 (−0.24, 0.34)	0.06	0.33	1.60 (0.54, 2.67)	0.14	0.03	1.39 (0.16, 2.95)	0.15	0.04
Emotional representation	1.11 (0.33, 1.88)	0.18	0.002	0.28 (−0.02, 0.58)	0.10	0.09	−0.10 (−0.36, 0.16)	−0.11	0.07	−0.13 (−1.11, 0.84)	0.002	0.98	−0.28 (−1.75, 1.18)	−0.05	0.50
BMQ necessity	0.60 (−0.06, 1.21)	0.13	0.03	0.24 (−0.004, 0.49)	0.09	0.10	0.11 (−0.10, 0.33)	0.04	0.49	−0.28 (−1.07, 0.50)	−0.06	0.33	−0.08 (−1.16, 1.01)	−0.12	0.12
BMQ concern	0.08 (−0.48, 0.64)	0.06	0.32	0.05 (−0.16, 0.27)	0.03	0.64	0.006 (−0.18, 0.19)	−0.02	0.74	−0.31 (−0.99, 0.38)	−0.002	0.97	−0.48 (−1.45, 0.49)	−0.03	0.69
HADS anxiety	0.48 (−0.012, 0.95)	0.09	0.11	0.14 (−0.05, 0.32)	0.08	0.15	−0.10 (−0.25, 0.06)	−0.05	0.40	−0.55 (−1.12, 0.03)	−0.12	0.04	−0.49 (−1.39, 0.41)	−0.15	0.05
HADS depression	0.90 (0.40, 1.40)	0.18	< 0.001	0.20 (−0.002, 0.40)	0.09	0.11	−0.13 (−0.30, 0.04)	−0.07	0.21	−0.27 (−0.90, 0.35)	−0.05	0.39	−0.04 (−1.05, 0.97)	−0.02	0.77

* IPQ = Illness Perception Questionnaire; BMQ = Beliefs about Medicines Questionnaire; HADS = Hospital Anxiety and Depression Scale; VAS = visual analog scale; TJC28 = 28 tender joint count; SJC28 = 28 swollen joint count; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; 95% CI = 95% confidence interval.

standing of additional factors that may affect each component is crucial.

Illness perceptions have been shown to be related to a number of outcome measures in RA, including disability, low mood, and poor physical functioning (11–14). To our knowledge, however, only one previous study has investigated the role of treatment beliefs with the main disease activity measure in 125 patients with RA, albeit using the full version of the Revised IPQ, but in that case, the researchers did not detect any associations with the total DAS28 (12). In the present study, we have shown that strong beliefs in negative consequences of RA, together with beliefs of more severe symptoms, were significantly associated with total DAS28. Furthermore, stronger associations were found for the subjective components of the DAS28 such as the TJC and, particularly, the VAS. One explanation is that patients use the VAS to communicate to physicians about their illness experiences and the impact that RA is having. Recording VAS scores separately could provide a useful way for clinicians to gauge the most appropriate treatment plan, which may be to target psychological as well as physical aspects of RA.

It was notable that more than one-quarter of the sample reported the highest levels of anxiety and one-fifth reported the highest levels of depression. Mood influences outcomes in a number of conditions, including diabetes mellitus (27) and myocardial infarction (28), through both direct and indirect routes, including motivation to engage in self-care activities. In the current study, no strong associations were found between total DAS28 scores and anxiety or depression; however, depression was significantly associated with the patient VAS. Anxiety and depression scores were significantly correlated with all of the Brief IPQ domains except timeline, suggesting that a complex pathway with an indirect effect upon outcome may be in use. Recognition of relationships between mood and illness cognitions gave rise to the use of cognitive–behavioral therapy (CBT) as an intervention for patients with RA. In the current study, the cross-sectional design precludes us from making claims about the direction of these influences; however, according to the Common-Sense Model (8), these are likely to be indicators of bidirectional relationships. Anxiety or depression may affect how a patient perceives their illness, or equally, illness perceptions could influence how anxious or depressed a patient becomes. These relationships may be moderated by other factors such as level of social support or presence of additional comorbidities, which have not been accounted for in the present study.

The high levels of anxiety and depression found in this sample of may indicate that screening for these factors for patients with severe disease should be routine. This is particularly important given that psychological distress in people with RA independently predicts discontinuation of anti-TNF therapy (29) and even mortality (17), but without active screening, depression may be missed (30,31).

Joint tenderness can be viewed as a subjective sign, being dependent upon the pain threshold of the individual, the strength of the pressure (stimulus) applied, as well as other influences, and has the potential to be confounded by both the patient and the clinician. From previous research on pain reporting and mood, we had anticipated that depression or anxiety would be positively correlated

Table 6. Linear regression analysis of associations between anxiety and depression and Brief IPQ items*

	Anxiety (range 0–21)			Depression (range 0–21)		
	β	**95% CI**	***P***	***β***	**95% CI**	***P***
IPQ domain						
Consequence	0.68	0.39, 0.97	< 0.0001	1.00	0.75, 1.25	< 0.0001
Timeline	−0.05	−0.40, 0.29	0.76	−0.10	−0.42, 0.21	0.51
Personal control	0.21	0.02, 0.40	0.035	0.23	0.06, 0.40	0.0079
Treatment control	0.36	0.08, 0.65	0.013	0.41	0.15, 0.66	0.0018
Identity	0.71	0.38, 1.04	< 0.0001	0.91	0.63, 1.20	< 0.0001
Concern	0.70	0.47, 0.92	< 0.0001	0.53	0.32, 0.73	< 0.0001
Coherence	−0.06	−0.27, 0.14	0.54	0.20	0.01, 0.38	0.037
Emotional representation	0.92	0.76, 1.07	< 0.0001	0.76	0.62, 0.91	< 0.0001
BMQ necessity	0.05	−0.1, 0.20	0.49	−0.01	−0.15, 0.13	0.87
BMQ concerns	0.29	0.16, 0.41	< 0.0001	0.18	0.06, 0.30	0.0028

* IPQ = Illness Perception Questionnaire; 95% CI = 95% confidence interval; BMQ = Beliefs about Medicines Questionnaire.

with TJCs (32,33); however, this was not found to be the case. These results replicate those found in a smaller study of depression and RA (19) and support the idea that TJC is not influenced by mood. Interestingly, however, TJC was significantly negatively correlated with illness coherence (understanding of disease). A higher TJC was associated with lower understanding of the condition. Illness coherence scores were surprisingly low in this sample of patients with a mean disease duration of 7.6 years.

Three item scores from the Brief IPQ correlated with ESR or CRP level; the strongest of these was the illness identity item, which assesses the degree to which patients experience symptoms. For the patients with severe disease in this study, this high correlation may reflect both the objective and subjective experience of high levels of current disease activity.

Results from the current study provide insight into patients' beliefs about the necessity of their medicines. One interesting finding was that, although patients believed they needed treatment, they had low confidence in the effectiveness of therapies available. It should be noted that the patients in the current cohort were recruited while awaiting anti-TNF therapy. Therefore, by virtue of the eligibility criteria for anti-TNF drugs, they had very active disease, which at this time had not been adequately controlled by previous treatment regimens. This may explain why confidence in medicines was low.

One of the strengths of the current study is that it included more than 300 study participants with severe disease, making it the largest of its type to date in RA. Unfortunately, because of the nature of recruitment across multiple sites, we were not able to ascertain the number of individuals who initially refused to take part; however, in an associated study involving a similar population of people with severe RA, 79% of those who were approached participated (34). Although we cannot rule out self-selecting bias, this information gives us a reason to think our sample was likely to be representative of this population.

A further strength of this study is the comprehensive set of questionnaires used to investigate relationships between psychological factors and disease activity. However, no correction for multiple testing was applied, meaning that some of the significant relationships identified may have arisen by chance; corroboration of these findings in an independent cohort is needed to substantiate these assertions. In addition, although the Brief IPQ was validated in a study of more than 500 participants (21), the measures of illness beliefs reported in this study mainly rely on single items that could potentially reduce reliability of these assessments.

We also needed to consider the possibility that correlations between variables for which data are collected via similar methods may be inflated due to shared methods variance. However, the fact that many of the self-report variables were not significantly correlated with each other was an indication that this was not a major consideration in this analysis.

Future analysis of longitudinal data would enable further assessment of the stability and direction of relationships between variables over time, as well as allowing identification of key mediators and moderators of those relationships. Previous research has supported the sensitivity and specificity of the total DAS28 for assessing disease activity. This study indicates that reporting and analyzing individual components separately may provide additional useful information to guide clinicians and researchers by indicating which aspects of the disease experience are being targeted by treatments, and this research team will monitor the impact of treatment on individual components in the followup date currently being collected. We cannot infer direction or causality from a cross-sectional study but, should the same results be found in a prospective analysis, it could help to identify a group of patients who may benefit from "adjunct" CBT. CBT has been shown to be effective in helping patients with RA to understand and adapt to living with the illness (35,36), although overall findings have been mixed, possibly because of the heterogeneity of CBT approaches. The findings in the present study suggest that a CBT approach that focuses on modifying illness-related dysfunctional schemata or beliefs may better address the needs of patients with RA and yield stronger and more sustained improvements in adjustment and disease-related outcomes. These findings may also stimulate research in other inflammatory diseases such as Crohn's disease or psoriasis, where sim-

ilar composite disease activity scores are used to assess eligibility and response to anti-TNF drugs.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Barton had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Cordingley, Plant, Ann W. Morgan, Isaacs, Barton.

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REFERENCES

1. Prevoo ML, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight–joint counts: development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995;38:44–8.
2. Kirby B, Fortune DG, Bhushan R, Chalmers RJ, Griffiths CE. The Salford Psoriasis Index: an holistic measure of psoriasis severity. Br J Dermatol 2000;142:728–32.
3. Hill S, Dziedzic K, Thomas E, Baker SR, Croft P. The illness perceptions associated with health and behavioural outcomes in people with musculoskeletal hand problems: findings from the North Staffordshire Osteoarthritis Project (NorStOP). Rheumatology (Oxford) 2007;46:944–51.
4. Hale ED, Treharne GJ, Kitas GD. The Common-Sense Model of self-regulation of health and illness: how can we use it to understand and respond to our patients' needs? Rheumatology (Oxford) 2007;46:904–6.
5. Leventhal H, Meyer D, Nerenz D. The commonsense representation of illness danger. In: Rachman S, editor. Contributions to medical psychology. New York: Pergamon Press; 1980. p. 17–30.
6. Leventhal H, Nerenz D, Steele D. Illness representations and coping with health threats. In: Baum A, Taylor S, Singer J, editors. Handbook of psychology and health. Vol. 4. Hillsdale (NJ): Erlbaum; 1984. p. 219–52.
7. Leventhal H, Diefenbach M, Leventhal EA. Illness cognition: using common sense to understand treatment adherence and affect cognition interactions. Cognit Ther Res 1992;16:143–63.
8. Leventhal H, Brissette I, Leventhal E. The commonsense model of self-regulation of health and illness. In: Cameron L, Leventhal H, editors. The self-regulation of health and illness behaviour. London: Routledge; 2003. p. 42–65.
9. Scharloo M, Kaptein AA, Weinman JA, Hazes JM, Breedveld FC, Rooijmans HG. Predicting functional status in patients with rheumatoid arthritis. J Rheumatol 1999;26:1686–93.
10. Carlisle AC, John AM, Fife-Schaw C, Lloyd M. The self-regulatory model in women with rheumatoid arthritis: relationships between illness representations, coping strategies, and illness outcome. Br J Health Psychol 2005;10:571–87.
11. Groarke A, Curtis R, Coughlan R, Gsel A. The impact of illness representations and disease activity on adjustment in women with rheumatoid arthritis: a longitudinal study. Psychol Health 2005;20:597–613.
12. Graves H, Scott DL, Lempp H, Weinman J. Illness beliefs predict disability in rheumatoid arthritis. J Psychosom Res 2009;67:417–23.
13. Scharloo M, Kaptein AA, Weinman J, Hazes JM, Willems LN, Bergman W, et al. Illness perceptions, coping and functioning in patients with rheumatoid arthritis, chronic obstructive pulmonary disease and psoriasis. J Psychosom Res 1998;44:573–85.
14. Sharpe L, Sensky T, Allard S. The course of depression in recent onset rheumatoid arthritis: the predictive role of disability, illness perceptions, pain and coping. J Psychosom Res 2001;51:713–9.
15. Isik A, Koca S, Ozturk A, Mermi O. Anxiety and depression in patients with rheumatoid arthritis. Clin Rheumatol 2007;26:872–8.
16. Zyrianova Y, Kelly BD, Gallagher C, McCarthy C, Molloy MG, Sheehan J, et al. Depression and anxiety in rheumatoid arthritis: the role of perceived social support. Ir J Med Sci 2006;175:32–6.
17. Ang DC, Choi H, Kroenke K, Wolfe F. Comorbid depression is an independent risk factor for mortality in patients with rheumatoid arthritis. J Rheumatol 2005;32:1013–9.
18. Kessler R, Berglund P, Demler O, Jin R, Koretz D, Merikangas K, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). JAMA 2003;289:3095–105.
19. Murphy H, Dickens C, Creed F, Bernstein R. Depression, illness perception and coping in rheumatoid arthritis. J Psychosom Res 1999;46:155–64.
20. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315–24.
21. Broadbent E, Petrie KJ, Main J, Weinman J. The Brief Illness Perception Questionnaire. J Psychosom Res 2006;60:631–7.
22. Horne R, Weinman J, Hankins M. The Beliefs about Medicines Questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health 1999;14:1–24.
23. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:361–70.
24. Neame R, Hammond A. Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. Rheumatology (Oxford) 2005;44:762–7.
25. Dickens C, McGowan L, Clark-Carter D, Creed F. Depression in rheumatoid arthritis: a systematic review of the literature with meta-analysis. Psychosom Med 2002;64:52–60.
26. Sheehy C, Murphy E, Barry M. Depression in rheumatoid arthritis: underscoring the problem. Rheumatology (Oxford) 2006;45:1325–7.
27. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. Arch Intern Med 2000;160:3278–85.
28. Jiang W, Glassman A, Krishnan R, O'Connor CM, Califf RM. Depression and ischemic heart disease: what have we learned so far and what must we do in the future? Am Heart J 2005;150:54–78.
29. Mattey D, Mattey D, Dawes P, Hassell A, Brownfield A, Packham J. Effect of psychological distress on continuation of anti-tumor necrosis factor therapy in patients with rheumatoid arthritis. J Rheumatol 2010;37:2021–4.
30. Nicassio PM. The problem of detecting and managing depression in the rheumatology clinic [editorial]. Arthritis Rheum 2008;59:155–8.
31. Sleath B, Chewning B, De Vellis BM, Weinberger M, De Vellis RF, Tudor G, et al. Communication about depression during rheumatoid arthritis patient visits. Arthritis Rheum 2008;59:186–91.
32. Adler G, Gattaz WF. Pain perception threshold in major depression. Biol Psychiatry 1993;34:687–9.
33. Chiu YH, Silman AJ, Macfarlane GJ, Ray D, Gupta A, Dickens C, et al. Poor sleep and depression are independently associated with a reduced pain threshold: results of a population based study. Pain 2005;115:316–21.
34. Potter C, Hyrich KL, Tracey A, Lunt M, Plant D, Symmons DP, et al, BRAGGSS. Association of rheumatoid factor and anticyclic citrullinated peptide positivity, but not carriage of shared epitope or PTPN22 susceptibility variants, with anti-tumour necrosis factor response in rheumatoid arthritis. Ann Rheum Dis 2009;68:69–74.
35. Astin JA, Beckner W, Soeken K, Hochberg MC, Berman B. Psychological interventions for rheumatoid arthritis: a meta-analysis of randomized controlled trials. Arthritis Rheum 2002;47:291–302.
36. Sharpe L, Allard S, Sensky T. Five-year followup of a cognitive–behavioral intervention for patients with recently-diagnosed rheumatoid arthritis: effects on health care utilization. Arthritis Rheum 2008;59:311–6.