An Examination of Work Instability, Functional Impairment, and Disease Activity in Employed Patients with Rheumatoid Arthritis

ALYSSA MACEDO, STEPHEN OAKLEY, NICOLA GULLICK, and BRUCE KIRKHAM

ABSTRACT. ***Objective.*** To evaluate the relationship between the Disease Activity Score 28-joint count (DAS28), Health Assessment Questionnaire (HAQ), and Rheumatoid Arthritis-Work Instability Scale (RA-WIS); and to define thresholds for clinical assessments associated with moderate to high RA-WIS.

Methods. Employed patients with RA were evaluated using DAS28, HAQ, and RA-WIS during routine clinics. Relationships between these assessments were evaluated by simple correlation. Multiple linear regression modeling was performed using RA-WIS as an outcome variable and HAQ, DAS28, age, sex, occupation, and disease duration as input variables. Receiver-operating characteristic curves were then formulated to determine optimal DAS28, and HAQ cutoff points for RA-WIS ≥ 10, along with the odds ratio (OR).

Results. Ninety patients with RA completed the RA-WIS, which was moderately correlated with DAS28 (r =0.53) and HAQ (r = 0.66). Fifty-four percent of RA-WIS was explained by DAS28 (p = 0.002), HAQ (p = 0.001), and sex (p = 0.04). A DAS28 of 3.81 and HAQ of 0.55 were clinically important thresholds. High DAS28 and HAQ were associated with high RA-WIS (OR_{DAS} 14.17, OR_{HAQ} 25.13, $OR_{DAS+HAQ}$ 29.9).

Conclusion. Functional impairment and disease activity significantly and independently contributed to patient-perceived work instability risk. (First Release Jan 15 2009; J Rheumatol 2009;36:225–30; doi:10.3899/ jrheum.071001)

Key Indexing Terms:
RHEUMATOID ARTHRITIS WORK WORK INSTABILITY DISABILITY
HEALTH ASSESSMENT QUESTIONNAIRE OUTCOMES

Rheumatoid arthritis (RA) is a chronic, progressive, and disabling disease affecting between 0.5% and 1.0% of the adult population[1]. At the time of symptom onset about half are of working age[2]. Although some individuals with RA may be work-disabled prior to diagnosis[3], the greatest increase in work disability occurs in the first 3 years of disease[4]. The Early RA study (ERAS), a prospective longitudinal study, reported that 22% of participants who were employed at enrolment had stopped working after 5 years because of their RA[5]. At least one-third of individuals with RA will leave employment prematurely, although this may vary depending on socioeconomic factors[6]. This is a major concern, as participation in paid work is a major life role and source of identity for most adults[6]. Lack of these productive roles has a negative effect on overall health as defined by the World Health Organisation[7], as well as a significant economic burden on the individual and society[1].

Historically, work disability outcomes involved measurement of work loss, as either work days lost or the receipt of work disability financial benefits[6,8]. Recent research has shown that there is limited success in reducing work disability by intervening once work loss has occurred[9]. These data have generated a change in emphasis. The focus of outcome measurement and intervention is now changing to investigating how people with arthritis function in their work roles[8,10,11]. This shift in focus has led to the development of measures for screening those at risk of work disability or decreased productivity while still at work.

Until recently there were few measures available to evaluate patient-perceived work disability risk. The RA-Work Instability Scale (RA-WIS; Leeds Rheumatoid Arthritis Instability Scale, ©2001 The University of Leeds, all rights reserved) fills this gap by measuring the work instability risk of individuals while they are employed[12]. The RA-WIS is a screening tool for work instability: the consequence of a mismatch between an individual's functional ability and his or her work tasks that threatens the individual's continued

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Funded by The Guy's and St. Thomas' Charity.

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Accepted for publication August 8, 2008.

employment if not resolved[12]. Work instability can be seen as the precursor to work loss, with a fluctuating level that may be reversed.

The RA-WIS is a self-report measure that enables patients to indicate the extent to which their RA has affected them individually at work. Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) strongly supports using tools like the RA-WIS that consider the patient's perspective[8]. Using this tool, patients are identified as having a low, medium, or high risk of work instability, indicating a need for further intervention. Although work instability itself is an important outcome, the main weakness of this tool is that the predictive power of the RA-WIS for actual job loss remains unclear.

Currently, rheumatologists commonly use 2 standardized outcome measures, the Disease Activity Score 28-joint count (DAS28), which measures RA disease activity, and the Health Assessment Questionnaire (HAQ), which measures functional status. The relationship of these measures to work instability risk has not been researched. In addition, the relevance of predefined threshold levels of these measures commonly used to guide treatment, e.g., remission, low or high disease activity defined by the DAS28, to work instability is unclear. A greater understanding of these relationships may assist in provision of timely intervention to prevent work loss. In this study, we examined the relationship of the DAS28 and HAQ with the RA-WIS.

The objectives of our study were: (1) to evaluate the relationship between RA-WIS scores and a range of clinical assessments including DAS28, HAQ-Disability Index (HAQ-DI), age, sex, disease duration, and occupational category; and (2) to define thresholds for clinical assessments (DAS28, HAQ, and age) associated with moderate to high RA-WIS.

MATERIALS AND METHODS

Study design. This was a cross-sectional study examining 3 standardized quantitative measures, DAS28, HAQ, and RA-WIS, in a sample of employed patients with RA.

Patients. Patients with RA involved in part-time or full-time paid employment attending routine specialized inflammatory arthritis clinics, at Guy's and St. Thomas' NHS Foundation Trust, London, UK, were evaluated. Ethics approval was obtained from the Bexley and Greenwich Ethics of Human Research Committee.

Recruitment procedure and data collection. Employed patients with RA attending routine rheumatology clinics were offered an opportunity to complete the written questionnaires (the HAQ and RA-WIS) before seeing their rheumatologist. The DAS28 score was obtained independently by the treating rheumatologists. Demographic details were obtained from chart review. Patients were categorized as "white collar" (professional) if they were managers/senior officials, or involved in professional occupations, associate professional and technical occupations, or administrative and secretarial occupations. They were categorized as "blue collar workers" (manual labor) if they were involved in skilled trades occupations, personal service occupations, sales and customer service occupations, process, plant and machine operatives, or elementary occupations, based on the UK Standard Occupational Classification (SOC2000). Data were collected and scored by the research occupational therapist. Data were stored according to the Data Protection Act (1998).

Main standardized assessments. The RA-WIS is a self-administered written questionnaire used to screen for patient-perceived risk of work disability. It has been shown to have excellent test-retest reliability and good content and construct validity[13]. The questionnaire takes less than 5 min to complete by checking "yes" or "no" boxes in a series of 23 questions. A score is achieved by counting all the "yes" responses. The range of scores is between 0 and 23. A higher score indicates a higher risk of work disability. In validation of this tool, it was determined that a score of 10 or higher identified 82% of those needing vocational intervention[13]. Therefore for our study, a WIS $\geq$ 10 identified patients who were at increased risk of work instability, and a WIS $<$ 10 identified patients who were at low risk.

The DAS[14] is widely used to quantify disease activity and gauge response to treatment[15]. The DAS28 assesses 28 joints measuring tender joints (28T), swollen joints (28S), erythrocyte sedimentation rate (ESR), and a patient global assessment of their disease activity scored on a visual analog scale (VAS)[14]. The DAS28 scores range from 0 to 10, indicating the current activity of RA. By convention a DAS28 above 5.1 is regarded as indicating high disease activity, while a DAS28 below 3.2 indicates low disease activity. Remission is defined as a DAS28 lower than 2.6[14,16-18].

The HAQ-DI is a standardized, self-administered, written questionnaire developed to assess the extent of the patients' functional ability across 8 categories[19]. The highest score for each of the 8 categories is summed (range 0–24) and divided by 8 to yield a continuous scale (0–3) of functional disability index. A higher score indicates greater functional disability. For our study a cutoff of HAQ $\geq$ 1.0 indicated "impaired function" and a HAQ $<$ 1.0 indicated "good function" based on key research in the field[20,21].

Statistical analysis. First, the relationships between RA-WIS and clinical data (DAS28, HAQ, age, sex, disease duration, and occupation) were evaluated by Pearson correlation or t test. A further analysis was completed with multiple linear regression modeling using RA-WIS as the dependent output variable and HAQ, DAS28, age, sex, disease duration, and occupational category as input variables.

Second, receiver-operating characteristic (ROC) curves were constructed to empirically determine the optimal DAS28, HAQ, and age thresholds associated with moderate–high work instability (RA-WIS $\geq$ 10), along with the odds ratio (OR; odds of association). The performance of DAS28 and HAQ using these empirically determined thresholds was compared to other commonly used thresholds. These included the DAS28 threshold of 5.1 used to define "high disease activity," DAS28 of 2.6 used to define "remission," and the HAQ threshold of 1.0 used to define "severe functional impairment." The OR was used as a guide to the overall diagnostic performance.

These ROC curves provide an indication of optimal clinical thresholds to indicate patients with increased patient-perceived work disability risk. The curve considers all cutoff points that give a unique pair of values for sensitivity (proportion of individuals who are correctly identified as being at high risk of work instability) and specificity (proportion of individuals who are correctly identified as being at low risk of work instability). The ROC curve plots sensitivity against 1 minus the specificity (thus comparing the probabilities of a positive test result in those with and without work instability). The optimal cutoff point is located closest to the top left corner of the ROC curve, indicating maximum specificity and sensitivity.

RESULTS

Demographic summary and analysis of the relationships among DAS28, HAQ, and RA-WIS by simple correlation. Approximately 120 employed patients with RA attending routine specialized inflammatory clinics were approached over a 6-month period and 75% completed the RA-WIS. A total of 90 employed patients with RA completed the RA-

WIS; 78% (n = 70) were women and 22% (n = 20) were men. The mean age was 48.3 years (range 20–69). Data on disease duration were available for 86 patients (mean 9.7 ± standard deviation 8.8, range 0–38 yrs). Occupational classification was available for 77 (86%). These patients were categorized as blue collar 13% (n = 10) or white collar 87% (n = 67). DAS28 scores were available for 80 patients, HAQ for 79, and RA-WIS for 90. The mean DAS28 score was 3.67 ± 1.54 (range 0.80–7.00), mean HAQ 0.90 ± 0.74 (range 0–2.63), and mean WIS 8.97 ± 6.58 (range 0–22) (Table 1). Fifty-four percent (n = 49) of patients were at low risk of work instability (WIS < 10) and 46% (n = 41) were at risk (WIS ≥ 10). The correlation of RA-WIS with DAS28 was r = 0.53, p = 0.001, and with HAQ r = 0.66, p = 0.001. There was no correlation > 0.3 with any other variable: age (r = 0.004, p = 0.97), sex (r = –0.007, p = 0.95), disease duration (r = 0.16, p = 0.132), or occupational category (r = 0.09, p = 0.45). DAS28 correlated with HAQ (r = 0.56, p = 0.001) (Table 2).

An evaluation of the relationship between DAS28, HAQ, and RA-WIS by regression modeling. An initial multiple linear regression model containing all 6 input variables found that DAS28, HAQ, and sex significantly influenced RA-WIS (R^2 = 0.55). Removal of the 2 least-significant input variables (age and occupational category) improved the model only marginally (R^2 = 0.5536), leaving 4 input variables (DAS, HAQ, disease duration, and sex). Disease duration did not correlate significantly with RA-WIS. Addition of an interaction term (DAS28 × HAQ) improved the model marginally, but neither the new variable nor disease duration was significant. In the final model (Table 3), DAS28 and HAQ showed strong independent positive correlations with RA-WIS scores. Male sex was also independently associated with higher RA-WIS (p = 0.02). In this model, DAS28, HAQ, and sex explained 54% of the variability in RA-WIS scores (R^2 = 0.57; adjusted R^2 = 0.54).

Table 1. DAS28, HAQ, WIS, age, and disease duration data.

	n	Minimum	Maximum	Mean (SD)
DAS28	80	0.80	7.00	3.7 (1.5)
HAQ	79	0.00	2.63	0.90 (0.7)
WIS	90	0	22	9 (6.6)
Age, yrs	90	20	69	48.2 (11.6)
Disease duration, yrs	86	0	38	9.7 (8.8)

DAS28: Disease Activity Score 28-joint count; HAQ: Health Assessment Questionnaire; WIS: Work Instability Scale.

Table 2. Analysis of DAS28, HAQ, sex, occupation, age, disease duration, and WIS by simple correlation.

	n	r	p
DAS28	80	0.53	0.001
HAQ	79	0.66	0.001
Sex	90	–0.007	0.95
Occupation	77	0.088	0.45
Age, yrs	90	0.004	0.97
Disease duration, yrs	86	0.16	0.13

Defining thresholds for clinical assessments by ROC curve analysis. A ROC curve analysis (Figure 1 and 2) revealed the optimal DAS28 threshold, indicating work instability to be 3.81 (sensitivity 0.76, specificity 0.82, OR 14.17). A DAS28 threshold of 5.0 was less sensitive (0.41) but more specific (0.95), with a lower overall performance (OR 13.10) (Table 4). A DAS28 threshold of 2.6 was more sensitive (0.88) but less specific (0.51), with a worse overall performance (OR 7.58).

The optimal HAQ threshold of 0.55 yielded sensitivity of 0.92, specificity 0.68, and OR 25.13. A HAQ threshold of 1.0 was less sensitive for work instability (0.68) but more specific (0.78), with worse performance (OR 8.33). Having both a DAS28 of greater than 3.81 and HAQ greater than 0.55 defined the moderate-high RA-WIS group with high sensitivity (0.90) and specificity (0.76) and carried the strongest overall association with moderate-high RA-WIS (OR 29.87). There was no meaningful age threshold identified, and neither sex nor occupational status appeared to be associated with moderate-high RA-WIS.

DISCUSSION

Work disability is a well known consequence of RA. Recent research has shown that there is limited success in reducing work disability once work loss has occurred. Therefore there is a significant need to identify patients at risk of work loss and to intervene early. The RA-WIS is a novel patient-oriented assessment tool that measures patient-perceived work instability risk. Currently, the RA-WIS is infrequently used in rheumatology clinics. Rheumatologists commonly aim for disease remission (DAS28 ≤ 2.6) and reduction in functional impairment (HAQ < 1.0). However, a clear understanding of the relationship between these measures and any threshold values relevant to patient-perceived work instability risk is not available. Our study was the first to examine the relationship among disease activity (DAS28), functional impairment (HAQ), and work instability (RA-WIS). A greater understanding of these relationships may assist in provision of timely intervention to prevent work loss.

Table 3. Multiple linear regression for influences on Rheumatoid Arthritis-Work Instability Scale. Number of observations = 70, r^2 = 0.57, adjusted r^2 = 0.5364.

Input Variable	Coefficient (95% CI)	p
DAS28	1.27 (0.58, 3.03)	0.004
HAQ score	4.75 (3.69, 11.78)	< 0.001
DAS28 × HAQ	–0.71 (–1.64, 0.2)	0.123
Sex, male	3.16 (0.49, 5.83)	0.021
Disease duration	0.04 (–0.07, 0.16)	0.451
Constant	0.44 (–2.37, 3.25)	0.756

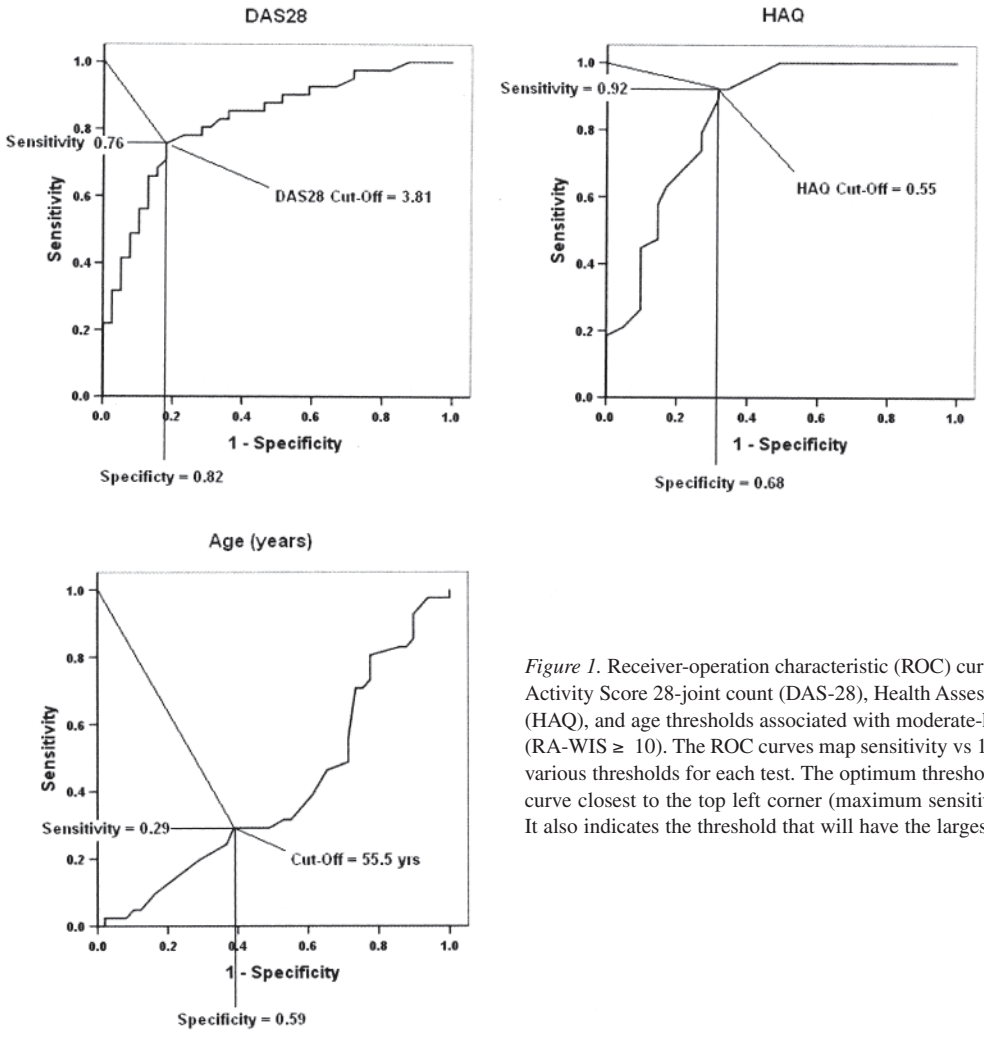

Figure 1. Receiver-operation characteristic (ROC) curves defining Disease Activity Score 28-joint count (DAS-28), Health Assessment Questionnaire (HAQ), and age thresholds associated with moderate-high work instability (RA-WIS ≥ 10). The ROC curves map sensitivity vs 1 minus specificity of various thresholds for each test. The optimum threshold is the point on the curve closest to the top left corner (maximum sensitivity and specificity). It also indicates the threshold that will have the largest odds ratio.

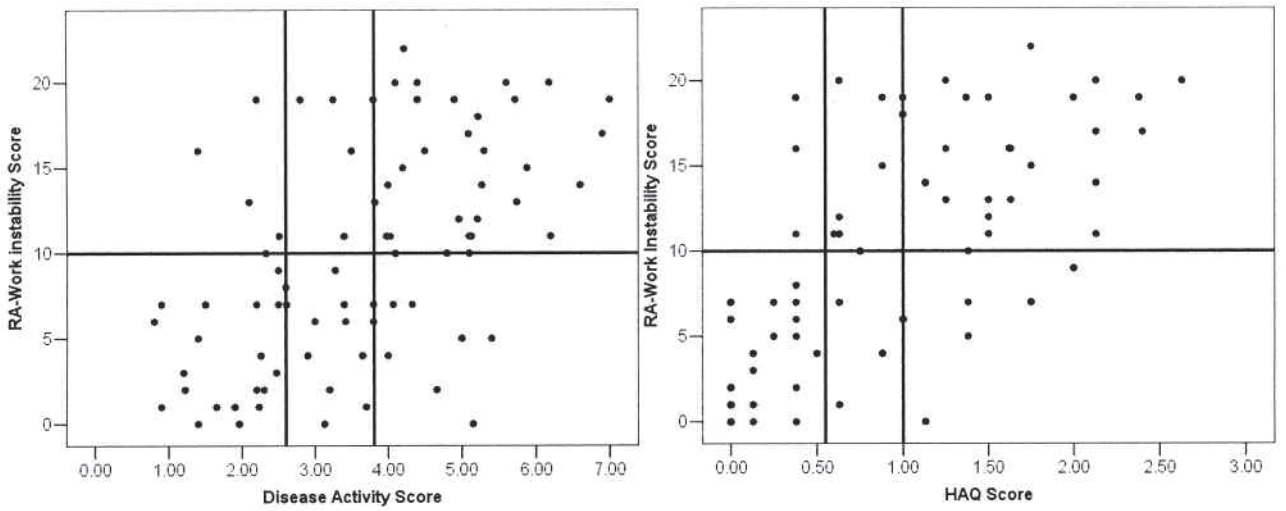

Figure 2. A comparison of Disease Activity Score 28-joint count (DAS28) and Health Assessment Questionnaire (HAQ) clinically meaningful cutoffs among patients with RA who are work-instable (RA-WIS ≥ 10). These scatter plots provide a useful visual representation of RA-WIS, HAQ, and DAS28 scores. They compare the newly proposed clinical thresholds for patient-perceived work disability risk (DAS28 > 3.81 and HAQ > 0.55) to the commonly accepted thresholds for actual work loss (HAQ ≥ 1.0 and DAS28 > 2.6). These findings illustrate that the probability of type I errors (false-positives) is lowered with a DAS28 > 3.81, and the sensitivity improved with a HAQ > 0.55.

Table 4. Clinical associations with work instability (RA-WIS ≥ 10).

Clinical Variable	Sensitivity	Specificity	OR (95% CI)
DAS28 > 3.81	0.76	0.82	14.17 (4.79, 41.93)
DAS28 > 5.00	0.41	0.95	13.10 (2.77, 61.90)
DAS28 > 2.60	0.88	0.51	7.58 (2.46, 23.38)
HAQ > 0.55	0.92	0.68	25.13 (6.51, 96.94)
HAQ > 1.00	0.68	0.78	8.33 (2.92, 23.72)
DAS28 > 3.81 and HAQ > 0.55	0.90	0.76	29.87 (7.47, 119.47)
Age > 55.5 yrs	0.29	0.59	0.65 (0.27, 1.58)
Sex, male	0.17	0.73	0.57 (0.20, 1.60)
Occupation, blue collar	0.70	0.85	0.91 (0.24, 3.45)

We found that DAS28 and HAQ both significantly and independently contributed to patient-perceived risk of work instability. RA-WIS scores were more strongly correlated to functional impairment (HAQ) than to disease activity (DAS28). This is supported by the literature, which consistently identifies work disability risk as more strongly related to functional scores than to measures of disease activity[20,21]. As the WIS and HAQ are both patient-derived measures relating to patient activities, it would be logical for this relationship to exist. There may have been less of a correlation with disease activity due to our particular patient demographic (more severe, more longstanding disease). It has been suggested that clinical disease characteristics are more important determinants of work loss in early RA, but the influence becomes less important over the years[22]. As our patient group had disease duration of years, those in more active jobs may have already lost employment. An inception cohort study is needed to answer this question, although our area is dominated by office-based employment.

Linear regression analysis illustrated that disease activity and functional status explained about half (54%) of the work instability measure. This is consistent with recent research illustrating that even though measures of disease activity and severity are important risk factors, they only partially predict risk of work disability[9]. Studies exploring work loss suggest that the remaining factors are made up of a complex interplay among individuals with RA, their occupation, and the environment[6]. One review of work disability risk and RA identified consistent predictors of leaving work prematurely as physically demanding work, lack of autonomy at work, higher levels of pain, lower functional status, and lower education level[21]. Many of these factors may increase risk of work disability for individuals regardless of their rheumatic disease or disease activity.

When considering the patient's perspective, a number of other factors have been identified that may contribute to variability in WIS. Patients identified fatigue as a more important threat than any other factor[6]. In a qualitative study, patients with RA identified 4 main areas for preventing work loss: reducing physical barriers to work, maintaining autonomy and ability to change practice in the workplace, maintaining social networks and ability to interact with employers and coworkers, and understanding patients' perspectives regarding motivation and work[23]. Therefore the factors not identified here contributing to variation in WIS scores may be explained by factors outside the remit of rheumatologists. This suggests there is an important role for a multidisciplinary team effort, e.g., occupational therapy or other vocationally oriented interventions, to improve these factors and subsequently reduce work disability.

The secondary objective was empirically to determine clinically meaningful thresholds of DAS28 and HAQ measures associated with work instability (RA-WIS). We found that a DAS28 threshold of 3.81 and a HAQ threshold of 0.55 had the highest sensitivity and specificity with RA-WIS values greater than 10.0. Clinically meaningful DAS28 and HAQ cutoffs have not previously been investigated in relation to measures of work instability such as the RA-WIS. When comparing our ROC data to the previously quoted targets of a DAS28 of 2.6 and HAQ of 1.0, which are predictive of actual work loss, they differ significantly[20,21]. Previous research has shown that the baseline HAQ score was the most important predictor of actual work disability[24].

As we were measuring work instability, potentially a precursor to work loss, it is logical that the HAQ threshold was lower and more sensitive to identify patients at an earlier stage of impairment. Conversely, the DAS28 cutoff was substantially higher than the previously proposed target. Since our sample consisted of a majority of non-manual workers, it is reasonable that the level was higher than previously proposed, as disease activity would likely affect work instability at a higher level compared to other studies including higher numbers of manual workers.

Our data concerning ROC-derived thresholds have some similarities to those derived from research into patient-defined acceptable levels of disease. The concept of patients reporting levels of disease at which they feel acceptably well is encapsulated in the patient-acceptable symptom-state (PASS)[25]. This concept has been evaluated to a small extent in RA. The largest study to date investigated patient-related and disease activity measures in 884 patients with RA of differing levels of disease activity, in relation to a standard question that asked if they felt their disease was at an acceptable level[26]. ROC curve analysis of a threshold of DAS28 levels for this patient-acceptable symptom-state gave a value of 3.84, remarkably similar to that found in our ROC analysis relating DAS28 to RA-WIS values of 3.81. That study showed that the most useful indicators of the PASS in those patients were patient-derived scores of global RA activity, with the least useful being measures of acute-phase reactants. These results support previous studies showing a divergence between disease activity measures, which often focus on inflammation, and patient-related outcome measures. In the above study[26] the threshold value for HAQ in relation to the PASS was 1.22, suggesting that our ROC

data, relating HAQ to RA-WIS values demonstrating a threshold of 0.55, show lower levels of impairment being reflected in patient concerns about work performance.

There were several limitations to our study. First, it should be remembered that the RA-WIS threshold of 10.0 has not been validated against actual work loss. Second, data were collected from a sample who were primarily white collar workers, typical of this geographical area; therefore, generalizability may be limited. Third, the effect of other variables was not collected in this preliminary study, i.e., employee support and work environmental issues, although these may have been helpful in determining the unexplained variation in RA-WIS. To resolve these limitations, further longitudinal, cross-site, larger studies are needed to determine the effect of the DAS28 and HAQ on WIS and the other variables involved.

Our study suggests that functional impairment and disease activity significantly and independently contribute to patient-perceived work disability risk. HAQ has stronger correlation to patient-perceived work instability risk, which is supported by the literature. As the HAQ and DAS28 explain only about half of the variability of the RA-WIS, other factors as discussed above are very important, suggesting that a multidisciplinary, vocationally-oriented approach would be useful to optimize work performance. ROC curve analysis showed that in a predominantly sedentary working population, a DAS28 $\leq$ 3.8 and a HAQ $\leq$ 0.55 were the most sensitive and specific thresholds relating to moderate to poor RA-WIS levels.

ACKNOWLEDGMENT

We thank Dr. Priscilla Harries, MSc, OT, Course Leader at Brunel University, for her valuable comments on the draft submission.

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