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# The consequences of rheumatoid arthritis: Quality of life measures in the individual patient

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**Key words:** Rheumatoid arthritis; pain; fatigue, depression, disability, health assessment questionnaire.

## ABSTRACT

Despite conventional treatment, RA still has many deleterious consequences. From the patients' perspective, these include persistent pain, functional disability, fatigue, and depression modified by health beliefs and underlying psychological problems. Disability is a consequence of pain, active synovitis and joint damage. It is usually assessed by self-reported questionnaire; the Health Assessment Questionnaire (HAQ) remains the dominant disability measure, although generic health measures such as Short Form-36 and Nottingham Health Profile provide similar information.

Treatment with disease modifying drugs and biologic agents improves pain, fatigue and disability. We specifically evaluated the effects of both these drugs and also disease duration on disability assessed by HAQ scores, as there is most information on this topic and it is of fundamental importance to patients. In early RA HAQ gives a 'J-shaped' curve; the initial fall is due to the immediate benefits of treatment and the subsequent gradual rise due to the inability of therapy to fully suppress the disease or prevent progressive joint damage. In established RA HAQ scores increase by about 1% annually and over 25 years average HAQ scores increase by 1.0. Disease modifying drugs and biologics both significantly reduce HAQ scores and the reduction is maintained for 2-5 years. This reduction is seen in both early and established disease. Early steroid therapy has immediate symptomatic treatment, but does not have long-term benefits. Over 5 years the impact of aggressive therapy with disease modifying drugs declines and there is evidence that insufficient treatment is given to many patients with RA.

The outcome of RA is greatly improved by current treatment with disease modifying drugs and biologic agents. How-

ever, more needs to be done and achieving better results is enhanced by routinely measuring the impact of the disease in routine practice.

## Introduction

As current treatment neither prevents nor cures rheumatoid arthritis (RA), the main management aim is to reduce the impact of the disease on patients' lives by improving quality of life and reducing disability. Clinicians consider that the most important effects of RA for patients are persistent pain and loss of function - attributable to the combined effect of continuing synovitis and progressive joint damage. However RA affects many aspects of individuals' lives and its impact extends beyond those areas traditionally considered to be within the domain of medical intervention. It is therefore complex to attempt to summarise in a succinct manner how RA affects individuals; its impact differs from case to case depending on a whole host of personal factors.

Historically, the impact of chronic diseases including RA on patients' lives has been defined in terms of three different levels defined by the World Health Organization: impairment, disability and handicap. In essence impairment is a loss of anatomical or psychological function, disability is an inability to perform normal activities due to impairment and handicap is the disadvantage for an individual resulting from an impairment or disability that limits the fulfilment of a normal role in life (1, 2). This overarching concept is now being superseded by the International Classification of Functioning, Disability and Health (the ICF framework) (3). This latter approach classifies patients' problems into four different components, which can be used to generate an individual code that is akin to that generated by the ICD-10 for the classification of disease. These four components comprise body functions and structures

(similar to the previous concept of impairment), activities and participation (similar to the previous concepts of disability and handicap), environmental factors, and personal factors. The first two components define functioning and disability, whilst the second two are regarded as contextual factors.

This review has a relatively modest aim of trying to summarise the impact of RA on individual patients. We cannot produce a scheme that will be universally relevant. However, the main areas of concern appear to be pain, fatigue, disability and depression. We have examined them in this order because it most closely represents a causal cascade. Pain and fatigue are essentially symptomatic consequences, which occur early in the disease and may remain constant throughout its course; disability is a result of the pain, inflammation and joint damage that characterise RA and develops early and gradually progresses; the psychological effects of RA appear to follow from the combination of pain and disability, mediated by individual patients underlying health beliefs and their pre-existing psychological status. We have also evaluated the effects of disease duration and treatment on disability assessed by HAQ scores, as there is most information on this topic and it is of fundamental importance to patients.

### Symptomatic consequences

#### Pain

Pain remains the major concern for most patients with RA. Its persistence is an important negative consequence of disease. Although controlling pain is one indication of successful treatment, the majority of RA patients have significant amounts of pain despite therapy.

**Measurement Instruments.** The most common way of measuring pain is the double anchored 100 mm visual analogue scale (VAS), labelled 'No pain at all' at one end, and 'Pain as bad as it could be' at the other end. The VAS was first developed in rheumatology in the 1970s by Huskisson *et al.* (4) and takes only a few seconds to complete. The pain VAS is part of the American College Rheumatology (ACR) and EULAR/OMERACT core data set (5, 6).

The verbal rating scale (VRS) is another simple measure which has been shown to correlate strongly with the VAS (7). The VRS consists of words which describe the severity of pain – such as 'none', 'mild', 'moderate', 'severe' and 'extreme'. This is not as widely used as the VAS although one study has shown that certain patients may prefer this to the VAS (8).

There are other more detailed pain questionnaires available which have been used in clinical studies and add much to the understanding of pain in RA. Their place in routine clinical practice is limited by the amount of time needed to complete the questionnaires. The McGill pain questionnaire (9) has 102 words in 20 categories and patients are asked to circle words that describe their current pain. The complete McGill pain questionnaire also has a diagram so that patients can indicate the location of their pain. There are also questions relating to the intensity of pain and how it changes with time. Although this questionnaire provides detailed knowledge and insight into the pain experienced in RA it takes at least 15-20 minutes to complete. Even the short version of the questionnaire (10) is too long to use in routine clinical practice but is useful in the research setting. The rheumatoid arthritis pain scale (RAPS) was designed specifically to measure pain in RA (11). This 24-item questionnaire has 4 domains and is measured using a seven-point Likert scale. Like the McGill questionnaire RAPS pro-

vides more information than the VAS but its use is limited to specialized clinical studies. Further information concerning measurement of pain is to be found in another chapter in this supplement.

**Impact.** Pain is one of the most common causes for patients to seek medical help (12-14). Almost all of the drugs currently used in arthritis, including analgesics, anti-inflammatory drugs, disease-modifying anti-rheumatic drugs (DMARDs) and biologicals, all target pain relief to a greater or lesser extent. However, despite such treatment, many patients continue to have considerable amounts of pain. The distribution of VAS pain scores in a typical clinical population of RA patients, many of whom are taking DMARDs and some who are receiving biologics, is shown in Figure 1. Pain scores are widely distributed over the whole range of severity and many patients have high or low scores. Patients with RA experience more pain compared with the population as a whole (15), and have similar levels to patients with widespread pain, though their disability levels are higher (16). Higher pain levels have been shown to correlate with disability (17) as well as depression (18), which all contribute significantly to a reduction in quality of life for patients with RA. Anti-inflammatory drugs are widely used in rheumatology, but there have been recent concerns over their use. Analgesics are frequently used but there has been little work exploring the

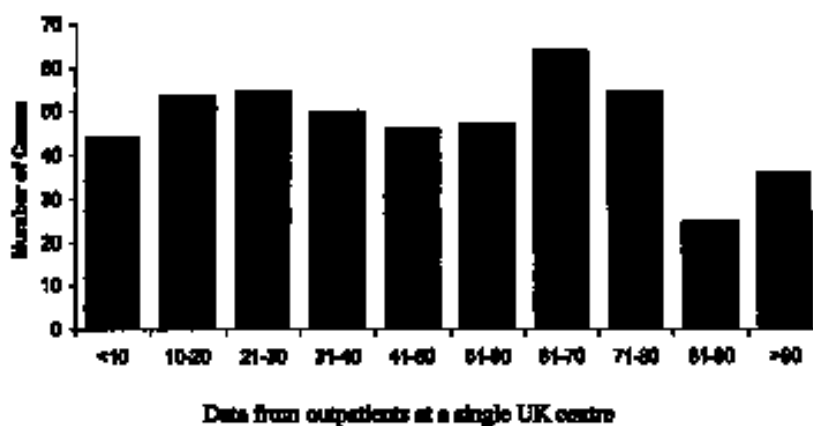


Fig. 1. Distribution of visual analogue pain scores in 471 RA patients (data from outpatients at a single UK centre).

benefits in RA, and qualitative research has shown that patients will self-prescribe over the counter analgesics as their pain is not well controlled. The course of pain follows the same pattern as many other measures of disease activity in groups of patients with RA; after an initial improvement, average pain scores gradually deteriorate with increasing disease duration.

### Fatigue

Clinically significant fatigue is present in 40-80% of patients with RA (19, 20). Patients regard fatigue as a major determinant of their quality of life (21) and disability (22). Qualitative research has confirmed that RA patients believe reducing fatigue should be a key treatment aim (23) and absence of fatigue is one of the components of remission, the principal therapeutic goal in RA (24). Despite these findings fatigue is not routinely measured in clinical practice or in studies.

**Measurement Instruments.** There is no agreement on the most appropriate measure of fatigue in RA, but the most commonly used instrument is the VAS. Like the pain VAS it usually takes the form of a double anchored 100 mm scale, labelled with 'No tiredness' at one end and 'Absolutely no energy at all' at the other end. This is a simple and easily reproducible method of measuring fatigue but does not capture the multidimensionality of fatigue in RA. There are a number of multidimensional instruments available that measure

fatigue but no consensus on the most appropriate instrument to use in RA. Most multidimensional instruments were designed for use in other chronic illnesses but have been applied to RA. Two of these measures have been validated in RA. The first of which is the multidimensional assessment of fatigue (MAF) by Belza *et al.* (25). This is a 16-item scale with 4 domains; severity, distress, degree of interference of daily living and timing.

The other validated instrument is the functional assessment of chronic illness therapy-fatigue scale (FACIT-F) (26), which has 13 questions with 4 domains; general, physical, mental fatigue and vigour. Other multidimensional instruments that have been used include an instrument developed for cancer (the MFSI) (27), the Chalder fatigue scale (28), and the fatigue symptom inventory (29). Generic health measures such as the SF-36 also have subscales (energy and vitality) that measure fatigue, though these are less specific. There are no reported head to head comparisons of all these instruments. However, Wolfe (30) has shown that the VAS performs well in comparison to the MAF, energy and vitality scale of the SF-36 and brief fatigue inventory, in terms of sensitivity to change and correlation with clinical variables.

**Impact.** Qualitative research has shown that fatigue is a significant problem for many patients with RA (31). The distribution of VAS fatigue scores in a typical clinical population of RA patients is

shown in Figure 2. In early RA, fatigue has been shown to be a dominant factor in determining quality of life and psychosocial aspects of daily living. The exact cause of fatigue in RA has not been established but several studies have shown that fatigue correlates most strongly with pain and depression (32, 33). Wolfe (34) has postulated the concept of 'fibromyalgic RA', based on the association of high regional pain scores and fatigue scores in some patients with RA. These patients had substantially worse quality of life. Clearly further work focusing specifically on fatigue in RA is needed.

### Disability and quality of life

#### Physical function

**Measurement Instruments.** The increasing focus on patients' perspectives of their health RA (35, 36) has resulted in an increasing interest in using health status measures to capture patients' views on their disease (37). Disability in RA is usually measured with self-assessment questionnaires. Most clinicians use disease-specific measures, such as the Health Assessment Questionnaire (HAQ) (38) or the Arthritis Impact Measurement Score (AIMS) (39). An alternative approach is to use generic measures; these include the SF-36 (40), the Nottingham Health Profile (NHP) (41) and the EuroQol (42). Although disease-specific measures are often preferred, generic measures discriminate across many RA severity categories (43) and can detect changes in early disease (44). Debate continues about how best to measure quality of life in RA and new measures are still being introduced (45). The advantage of generic measures is that disability in RA can be compared with other diseases (46), but such measures are relatively insensitive with significant ceiling and floor effects. Although the disease-specific measure, AIMS, is a good measure, it is complex and therefore has not been widely adopted. Overall HAQ has become the dominant assessment instrument. It is not only widely used in RA but is also informative in osteoarthritis, fibromyalgia and many other rheumatic diseases.

**HAQ Scores.** The range of HAQ scores

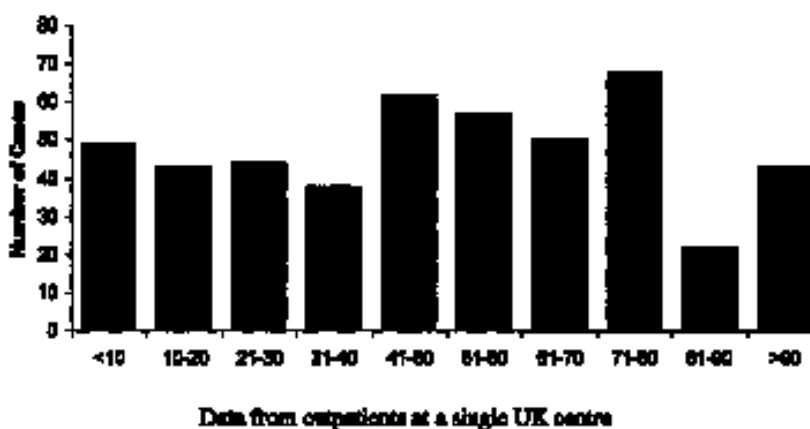


Fig. 2. Distribution of visual analogue fatigue scores in 471 RA patients (data from outpatients at a single UK centre).

in an outpatient group of RApatients attending our outpatient clinics is shown in Figure 3. These patients show a broad range of HAQ scores, with a substantial number having low scores. Although there are a number of variations in HAQ scores that can be collected, including the shortened modified HAQ (47) and the shortened RA-HAQ, a study by Wolfe (48) of 2,491 clinic patients with RAwith active disease showed the conventional HAQ is better at detecting treatment change, and identifies the extent of functional disability better than the shortened questionnaires. The benefits of the MHAQ and RA-HAQ are that they are short and easier to score. However, these benefits come at the price of loss of sensitivity and loss of sensitivity to change.

A more acceptable alternative has been developed termed the HAQ-II, which involved 10 items. This has been studied in 14,038 RA patients with rheumatic disease over a 2-year period (49). It is reliable, has a longer scale than the conventional HAQ, and may therefore be better equipped to avoid floor and ceiling effects. The HAQ-II performed as well as the HAQ in a clinical trial and in prediction of mortality and work disability. Conversion from HAQ to HAQ-II and from HAQ-II to HAQ for research purposes is simple and reliable. The HAQ-II can be used in all places where the HAQ is now used, and it may prove to be easier to use in the clinic.

Another modification of the HAQ is the multidimensional HAQ (MDHAQ), developed and validated in 688 patients by Pincus *et al.* (50). One of the prob-

lems of the MHAQ and HAQ as mentioned above is the floor effect. The MDHAQ by adding 6 advanced questions on activities of living (ADL) to the 8 ADL included on the MHAQ aimed to overcome this floor effect. Whereas patients may report no problems performing simple tasks, they may experience difficulty performing advanced tasks. Also psychological items which assess depression, anxiety and poor sleep which are included may be used to screen for these common problems. The MDHAQ has been subsequently revised (51) and the number of ADL items has been reduced to 10 items and was found to provide similar information to the 14 item MDHAQ but is more easily completed. The MDHAQ is a simple 2-page questionnaire that could be completed at every clinic visit and takes only seconds to score. It is likely that HAQ-II and MDHAQ will be widely used over the next few years. Another simplification in HAQ scores that has been suggested is using visual analogue scales to assess function. Wolfe and Michaud (52) studied 394 RA patients comparing HAQ, the HAQ-II, and a visual analogue functional scale. They found that the distribution differences between HAQ and HAQ-II and the VAS-F suggest that patients do not see minor limitations as problematic, but rate major limitations as being particularly limiting and worthy of high ratings. They concluded that a visual analogue functional scale, which represents a patient-weighted functional assessment in which additional interpretation is given to the meaning of the limitations by the pa-

tient, may be suitable for use in the clinic and in research.

There is debate about the value of HAQ for managing patients in routine clinical practice. A controversial study by Greenwood and her collaborators (53) examined changes in HAQ scores in 207 RA patients. They concluded that, as a general guideline, HAQ scores need to change by 0.48 points or more to be certain that this reflects a genuine clinical change of importance. An associated issue is the frequency of ceiling scores, which can mean that in severe RA the progression of HAQ scores under-estimates the overall worsening of the disease. This finding has been shown in a long-term study of 245 RA patients with late disease followed for 5 years, in whom the average rate of progression was 0.03 units per year (54). Interestingly a subsequent commentary on the value of HAQ by Wolfe and his colleagues (55) found that in 2,720 RA patients even larger changes were needed in ESR or joint counts to be certain that there had been a clinically important change, suggesting that interpreting change is complex and that the HAQ performs as well as other clinical measures, and may even perform better than most.

*SF-36 and NHP Profiles.* The SF-36 is the most widely used generic measure of health status. The SF-36 can be self-administered or with the use of an interviewer. It can be completed in 5-10 minutes and has been applied to large populations in a number of countries and to patients with a variety of illnesses of all age groups. There are 36 questions in the SF-36, these items are grouped into 8 scales; physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE) and mental health (MH). There are 2 summary measures which aggregate the 8 scales; Physical Health (PF, RP, BP, GH) and Mental Health (VT, SF, RE, MH). All but one of the 36 items are used to score the 8 SF-36 scales. Each item is used in scoring only one scale. These 8 scales were selected from the 40 used in the Medical Outcomes Study, those chosen were felt to represent the most frequently

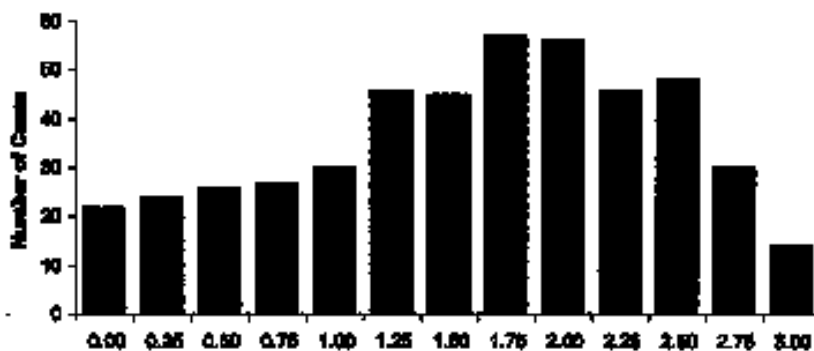
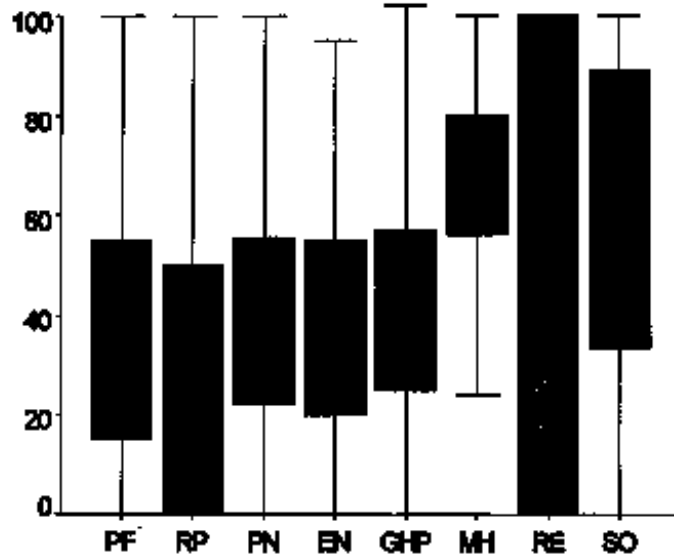


Fig. 3. Distribution of HAQ scores in 471 RApatients (data from outpatients at a single UK centre).

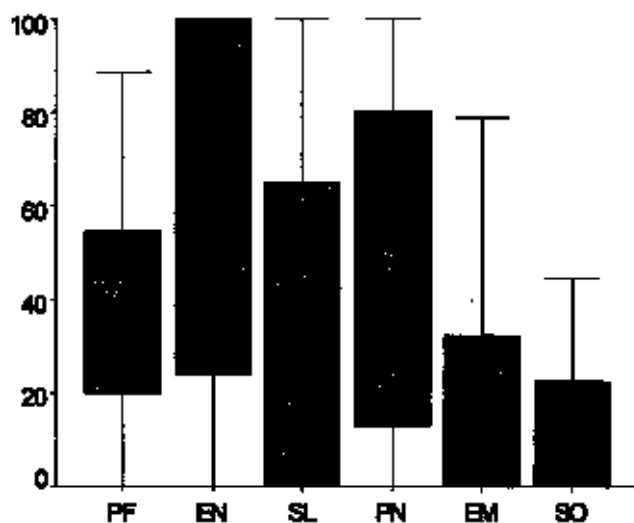


**Fig. 4.** Distribution of SF-36 scores in 321 RA patients. Domains comprise physical function (PF), role physical (RP), pain (PN), energy (EN), general health (GHP), mental health (MH), role emotional (RE) and social (SO). Data from outpatients at a single UK centre.

measured concepts in widely-used health surveys and those most affected by disease and treatment. A shortened version of 12 items [SF-12 (56)] has been developed but due to less precise scores can only really be used in large studies and also provides less information on health status and outcomes than the SF-36. The range of scores in the different domains of the SF-36 in current clinic attenders are shown in Figure 4.

There have been many previous studies

of SF-36 profiles in RA. Ruta and colleagues (57) reported that in 233 patients with RA the SF-36 scales were reliable, correlated with core disease activity measures and were responsive to improvements in health. Birrell and colleagues (58) studied 86 RA patients attending specialist clinics and found that impairment of health status was moderate to marked by the SF-36, with significant differences from population norms and chronic disease states such as low back pain. They concluded that



**Fig. 5.** Distribution of NHP scores in 321 RA patients. Domains comprise physical function (PF), energy (EN), sleep (SL), pain (PN), emotional (EM) and social (SO). Data from outpatients at a single UK centre.

it is a practical tool for use in patients with RA.

Although the NHP was initially designed as a 2-part questionnaire, only the first part is widely used as part 2 is not applicable to all responders. Part 1 which is commonly used consists of 38 statements which are grouped into 6 subscales; physical mobility, pain, sleep, emotional reaction, social isolation and energy. These statements were generated from large surveys of the general population. Each question has a yes or no answer, each being weighted according to perceived severity. There are a number of problems when using the NHP. Each statement has a simple yes or no question, limiting the subjects' response; the method of weighting the severity of items can give confusing results. There are also problems with floor and ceiling effects, improvements in those with minor ailments who started with a zero score may not be detected, those subjects who score maximally on an item will continue to have the same score despite any deterioration. The range of scores in the different domains of the NHP in current clinic attenders are shown in Figure 5.

There have also been a number of previous studies of the NHP. Houssien and colleagues (59) reported high scores for pain, physical mobility and energy level sections, and also considerable distress levels for sleep and emotional reactions. There were moderate associations between NHP scores and disease activity measures, including the number of tender and swollen joint. Not all studies found an impact on sleep and emotional reaction. For example, Uutela and colleagues evaluated 99 RA patients and found that NHP scores for mobility, pain and energy were very different from control values but sleep, emotional reaction and social isolation were similar between RA patients and controls (60). The association between abnormal NHP scores and disease activity is shown in all studies and was most recently confirmed by Sivas and colleagues (61), who reported that in 100 RA patients all subgroups of the NHP significantly correlated to pain and the articular index, but not with C-reactive protein levels.

*Other measures of quality of life*

In view of new and increasingly expensive treatments for RA, clinical studies often include economic evaluation in the form of cost-utility analysis. In this method a utility is used as a global, health related quality of life measure. A utility being the preference of patients for given states of health. It is expressed as a value between 0 (equal to death) and 1 (equal to full health). Thus, living 1 yr with a utility of 0.5 is equal to living half a year in full health. The three most widely used methods of utility measurement are the standard gamble (SG), the time trade off (TTO), and the VAS. With the SG, the respondent is asked to make a choice between two options. The first option is the certainty of living with a certain illness for the rest of one's life. The other option is a gamble with two possible outcomes, living for the rest of one's life in perfect health or immediate death. The chances in the gamble are varied to determine the point at which a subject is indifferent about the choice between the certain option and the gamble. The TTO asks the subject to value health states in terms of duration of life in a state of perfect health that would be equivalent to some period with a particular illness such as their own. In large populations, descriptive instruments such as the EuroQol (EQ-5D) are used.

The EuroQol is available in English and many other European languages. It is a validated quality of life questionnaire which has five questions based on mobility, self-care, usual activities, pain/discomfort and anxiety/depression, with three levels of answers (no/some/severe problems). From these five questions, descriptive health states were derived and assessed using TTO/SG to create a social tariff. However, the EuroQol has been criticised for its inability to detect therapeutic response and its rather restricted content.

**Physical function and anti-rheumatic therapy***Observational studies*

The majority of information in RA, in both early and late disease, comes from studies using the HAQ. Five year prospective studies the UK, Scandinavia

and continental Europe show that in early RA there is a 'J-shaped' curve, in which there is an initial fall in HAQ scores followed by a gradual increase (62-68). This J-shaped pattern is independent of the degree of initial disability, and occurs similarly in men and women, even though women have higher HAQ scores. The explanation for this 'J-shaped' curve is that patients with RA have considerable disability before they start treatment. Therapy with symptomatic agents and DMARDs initially improves synovitis and hence associated disability, but disability rises again slowly thereafter as joint damage and other disease manifestations progress in a manner that no longer responds to therapy. When HAQ changes are studied over shorter periods of time, it seems most of the early improvement occurs within the first 12 months (69). The likelihood of patients progressing to levels of significant disability in early RA – especially HAQ scores over 1.0 – is more likely if they have typical disease that is referred for hospital specialist care. This was shown in a UK community-derived cohort of 318 early polyarthritis patients (70). The 138 cases with typical RA that required hospital specialist care had a median HAQ score of 1.13 after 5 years compared with a median score of 0.75 in the whole cohort. Similar differences were seen when the SF-36 was used to assess the impact of RA with cases needing specialist care having worse physical function, less vitality and worse social functioning and emotional health.

In established RA, HAQ scores are correlated with disease duration; overall the longer the duration of RA the higher the HAQ score (71). Wolfe *et al.* (72) showed that in current clinic attenders with RA, the mean disease duration in those with HAQ scores of less than 1.0 was 7 years, while in those with HAQ scores of over 2.0 it was 14 years. One approach to examining the gradual worsening of disability is to calculate the average annual increase in HAQ scores. Leigh and colleagues (73) found an average annual increase in HAQ scores of 0.018 in 209 patients followed over 8 years, which increased to 0.045 when deceased patients were

counted as maximally disabled. Previous reviews have combined data from cross-sectional and longitudinal studies to show that the average increase in HAQ scores in RA patients attending outpatient clinics is 0.031/year (~1% of possible maximum disability) (74). This means that over 25 years the average HAQ score would increase by < 1.0.

*Trials in established RA*

HAQ scores are sensitive measures of effective DMARD therapy. Improvements in HAQ may be especially useful early in the treatment process to assess patients' responses to DMARDs. The relative importance of HAQ was shown by Scott and Strand in an analysis of the leflunomide clinical trial database (75). Evaluating results from 1817 RA patients enrolled in three trials that compared leflunomide, methotrexate and sulphasalazine showed that mean HAQ scores declined progressively with DMARD treatment. Changes occurred rapidly and correlated with clinical response. Regression analysis showed pain intensity and global assessments were the dominant determinants of HAQ. Interestingly further analysis of this data from the leflunomide trials showed that HAQ and other patient-reported assessments of disease activity were best at discriminating between active and placebo therapy compared to physician-reported measures such as joint counts (76). More long-term results from the leflunomide database showed that improvements in physical function were sustained over 24 months of successful treatment with DMARDs (77).

HAQ is equally responsive to changes in disease state when combination therapy is used. This has been shown in the leflunomide-methotrexate study in which patients who had persistently active RA despite receiving methotrexate for at least 6 months were treated with additional leflunomide or placebo (78) with a subsequent open-label extension (79). HAQ scores improved with active treatment and remained lower over 12 months in patients who remained on therapy.

HAQ shows major improvements when

patients receive anti-TNF therapy. A systematic review of the early trials of anti-TNF is shown in Figure 6, derived from the National Institute for Clinical Excellence in the UK ([www.nice.org.uk](http://www.nice.org.uk)). This summary showed changes in HAQ score in the region of 0.4 with etanercept, infliximab, and adalimumab. For example, one 12 month trial involving 619 patients with active RA who had an inadequate response to MTX showed highly significant improvements in HAQ with mean changes of 0.61 with the highest dose of the anti-TNF (80). Routine practice studies show similar falls in HAQ scores, though their magnitude is somewhat less than in clinical trials; for example Bennett *et al.* showed falls in HAQ of 0.34 with adalimumab (81).

Long-term follow up studies have evaluated changes in HAQ scores over 3 years in early and late RA. Patients in both groups showed rapid and sustained clinical responses with etanercept therapy, but patients with recent onset RA showed significantly greater improvement in HAQ scores compared with patients with established RA. The difference in magnitude of HAQ score improvement between groups was observed as early as week 2 after initiation of etanercept and persisted throughout the 3-year time frame (82).

#### *Trials in early RA*

There has been an intensive focus on trials in early RA. These include trials of low-dose steroids, DMARDs given singly or in combination and biologics. The studies with low-dose steroids, particularly the ARC-trial led by Kirwan (83) represented an important change in this field of research. Although the main focus was on x-ray progression the study also showed important falls in HAQ scores with treatment, though there were no major differences between therapeutic groups. The other key trial in this area, the Cobra trial led by Boers (84) showed that low dose early steroids had a long-term benefit on joint damage and a more difficult to assess impact on long-term functional changes, particularly after 5 years of RA (85). Although there was a substantial improvement in

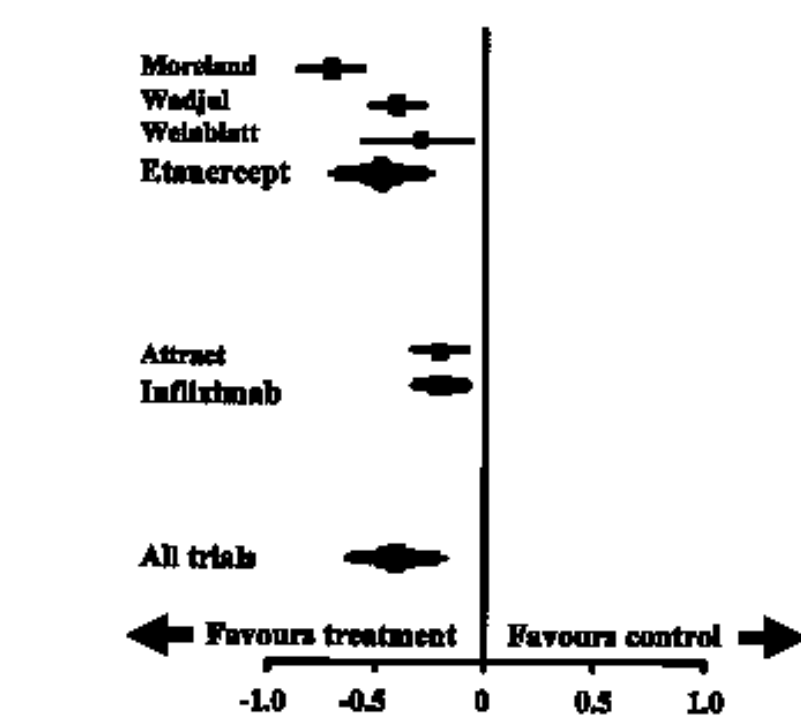


Fig. 6. Systematic review of changes in HAQ in anti-TNF trials.

HAQ scores compared to initial values and this improvement was maintained for the next 5 years. However, there were no differences between treatment groups during this time.

The results of the Fin-RACo trial (86), in which patients had more aggressive therapy with a combination of two DMARDs – methotrexate and sulphasalazine – often combined with steroids showed that combination therapy resulted in a significant fall in HAQ scores over 5 years (87). By contrast Maillefert and colleagues (88) compared early combined treatment with methotrexate and sulfasalazine with monotherapy during the first year in early RA. After 5 years they found no evidence that early combination therapy influenced long term disability, or indeed other components of the disease process.

Finally Verstappen and colleagues (89) examined the long-term functional benefits of initial aggressive DMARD therapy compared to the classical pyramidal approach starting with symptomatic treatment. Although there was a substantial early benefit, by 5 years this advantage had ceased. They suggest more aggressive treatment ap-

proach is needed in early RA and that treatment should be continued for a prolonged period of time, in order to maintain the advantages obtained in the first year.

#### **Psychological impacts**

*Measurement Instruments.* There are many different instruments that have been designed to assess depressive symptoms, such as the Hospital Anxiety and Depression score (90) and the Beck Depression Inventory (91). Despite the fact that these symptoms are common in patients with RA, they are very rarely documented or assessed in clinical practice and are only assessed in specialised studies.

*Impact.* Depression, which is often associated with high levels of fatigue, has been identified as a problem for a large proportion of patients with RA (92) and some studies have suggested that depressive symptoms are present in 25% or more of patients (93). Many patients also have high levels of anxiety (94). Depression has been shown to be associated with reduced health status, as well as higher pain and fatigue levels and reduced quality of life (95). RA often causes chronic pain and the effects

of chronic pain on patients' physical, psychological and social functioning has been widely recognised (96). Other factors other than pain have been found to be important in psychological adjustment in patients with RA. Specifically social support is particularly significant in adjustment to RA given the limitations that physical disability may create. Social support has been found to minimize the effects of physical limitations resulting from RA (97,98). The situation is further complicated by RA patients with a pre-existing history of an affective disorder such as depression; who have higher levels of fatigue and ill health, with self-efficacy playing an important mediating role in this relationship (99).

Pain and disability inevitably affect patients' psychological status and general feeling of well-being. Although there is no evidence that patients have primary psychological disturbances, chronic illness may cause substantial long-term psychological effects. In a large study by Polsky *et al.* (100) they examined the risk of developing significant depressive symptoms following a new diagnosis of a chronic illness over a 6-year period. In all illnesses there was a high risk of depressive symptoms developing in the first 2 years after diagnosis, although the risk decreased after this period. However, in patients with arthritis there was a significantly higher risk of developing depressive symptoms 2-4 years after diagnosis.

Comparative studies of different chronic diseases show that psychological functioning contributed to overall quality of life for all disorders, whereas physical and social functioning contributed in only some diseases (101). The relationship between disability and psychological morbidity is thus relatively specific for RA. Interestingly illness perceptions, which are an individualistic view of disease, may be key factors in determining the impact of RA (102), which has been shown in a small study of 75 women with RA. Depression was found to be associated with high use of coping by denial and with less frequent use of active coping, planning and seeking instrumental social support. It appears that illness perceptions have

significant implications for adaptation to illness and outweigh the impact of medical disease status on depression, physical function and pain.

### Conclusions

Despite treatment RA continues to have deleterious consequences on pain, fatigue, physical function, depression and associated psychological features and disability. Pain and fatigue do not necessarily progress over the course of RA. In contrast disability, which is a consequence of pain, active synovitis and joint damage, worsens in most cases. It is invariably assessed using self-reported instruments with HAQ remaining the dominant measure.

In early RA, HAQ gives a 'J-shaped' curve; the initial fall is due to the immediate benefits of treatment and the subsequent gradual rise due to the inability of therapy to fully suppress the disease or prevent progressive joint damage. In established RA HAQ scores increase by 1% annually and over 25 years average HAQ scores increase by 1.0. Disease modifying drugs and biologics both significantly reduce HAQ scores and the reduction is maintained for 2-5 years. This reduction is seen in both early and established disease. Early steroid therapy has immediate symptomatic treatment, but does not have long-term benefits. Over 5 years the impact of aggressive therapy with disease modifying drugs declines and there is evidence that insufficient treatment is given to many patients with RA.

Although the outcome of RA can be markedly improved by treatment with DMARDs and biologics, therapy is not ideal. Many RA patients still have significant symptoms and considerable disability. More needs to be done and achieving better results will depend on routinely measuring the impact of the disease in routine practice. All specialists should routinely record patient-focused outcomes within routine care.

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