Patient Outcomes in Rheumatoid Arthritis
Shared decision-making between the patient, clinicians and other healthcare professionals has been recognised as a fundamental part of the treatment strategy for rheumatoid arthritis. Clinical remission is the primary target of treatment, although low disease activity is considered to be an acceptable alternative, particularly if the patient has long-standing disease. Recommendations from an international task force emphasise the importance of giving patients information about the potential benefits and risks of treatment in order to achieve the treatment target.

In 2011 an international steering group of rheumatologists and patients developed a patient version of the original recommendations from the task force (published in 2010) to facilitate the shared decision-making process and support treatment adherence. Ensuring the patient is well informed about the risks of having rheumatoid arthritis, the implications of tight control as a treatment strategy and anticipated outcomes is important for achieving adherence. However, there is evidence to suggest that patients and clinicians differ in their assessment of treatment outcomes and disease activity. Discrepancies between patients’ and clinicians’ assessments of physical function have been a long-standing concern.

The impact of rheumatoid arthritis on patients’ quality of life
A small qualitative study involving 25 patients with rheumatoid arthritis in Sweden looked at the outcomes from treatments that patients considered to be the most important in terms of their quality of life and general well-being. The researchers held focus groups at four hospitals. Outcomes that patients identified as being the most important to them included:

- being able to live a “normal” life and regain full health. Patients did not want to feel limited in their ability to carry out household tasks or participate in social activities.
- a reduction in pain and stiffness and an increase in mobility. Patients also mentioned the impact of fatigue on their physical capacity and some patients mentioned that they felt unable to do anything because of fatigue.
- maintaining their independence – patients emphasised the importance of being able to manage daily tasks such as dressing themselves, managing the household, caring for their families and managing work.

In another small qualitative study that evaluated the possible reasons for discrepancies between patients’ and clinicians’ perceptions of disease activity, patients mentioned that they often avoided participating in certain activities because they knew that the activities would cause pain. They felt that having to make adjustments in their daily life was a loss. Some patients felt that medical treatment had a negative impact on their general well-being and they thought that the side effects of treatment were a possible cause of fatigue.

The development of patient-reported outcomes
The ability to accurately assess the extent of disease activity is crucial for determining the severity of disease and monitoring the effects of treatment in patients with rheumatoid arthritis. Concordance between patients’ and physicians’ assessments of the activity of disease is vital if patients are to be managed safely and effectively. The assessment of the severity of disease is dependent on subjective measures (e.g. how the patient thinks their arthritis is progressing) as well as objective measures (e.g. the number of swollen joints, the levels of acute phase reactants). Patient-reported outcomes (PROs) are becoming increasingly important in trials and clinical practice because they provide information about how the patient views specific aspects of their disease and their overall health. The emphasis on shared decision-making and consideration of the patient’s perception of health when developing management plans means that PROs may have a key role to play in the routine assessment of patients in clinical practice (as well as providing an outcome measure in clinical trials).

The development of core sets of variables and indexes, such as the Disease Activity Score (DAS), that combine objective measures with PROs has helped to facilitate the standardised measurement of disease activity in clinical trials. The value of involving patients in the development of patient-reported outcome measures has recently been recognised. For example, fatigue is now considered to be an important outcome measure. One study found that 80% of patients suffer with fatigue and over 50% have high levels of
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fatigue. At a series of OMERACT conferences patients highlighted that healthcare professionals did not appear to recognise that fatigue was a significant symptom for them. As a result of these discussions fatigue is now recognised as an important outcome measure to consider in clinical trials.

The potential effects of discordance in clinical practice

If there is discordance between clinicians’ and patients’ assessments of disease activity and severity it may affect the shared decision-making process and the effectiveness of treatment. Discrepancies between assessments of disease activity may lead to conflict, between which outcome measure should be guiding decisions about treatment. Discordance between perceptions of physical functioning could lead to healthcare providers recommending treatments for patients that are unnecessary or not recommending interventions for patients where needed.

What are the possible reasons for these discrepancies?

A longitudinal and cross-sectional study of 646 patients with rheumatoid arthritis who were taking methotrexate examined the possible causes for discordance between patients’ and clinicians’ assessments of disease activity.

The authors examined:

- variables that correlated with the Patient Global Assessment (PGA) and the Evaluators Global Assessment (EGA) (e.g. pain, swollen joints);
- the determinants of discrepancies between the PGA and EGA; and
- the determinants of discrepancies in improvement between the PGA and EGA.

There was a strong correlation between pain scores and the PGA \( r = 0.86, p < 0.001 \) and the number of swollen joints with the EGA \( r = 0.77, p < 0.01 \). A multivariate analysis found that pain explained 75.6\% of the variation in the PGA.

The following variables showed a significant association with the degree of discrepancy between the PGA and EGA scores:

- number of swollen joints \( r = -0.39 \);
- pain score \( r = 0.62 \);
- Health Assessment Questionnaire (HAQ) score \( r = 0.26 \);
- number of joints that were tender \( r = 0.15 \); and
- the duration of morning stiffness \( r = 0.21 \).

The negative correlation for swollen joints indicates that in patients with a higher number of swollen joints, clinicians had a worse perception of the severity of disease than the patients did. Pain scores and the number of swollen joints were the only variables found to be independently associated with discrepancies between the PGA and EGA \( p < 0.001 \).

The authors looked at proportional changes between the two scores and concordance in perceptions of changes in disease activity following treatment (i.e. whether disease activity had improved, worsened or remained the same). They found that:

- 42\% of patients thought disease activity was better after starting treatment and 45\% of clinicians thought the same;
- 37\% of patients thought there was no change in their disease activity compared to 27\% of clinicians; and
- 21\% of patients thought that disease activity had worsened compared to 28\% of clinicians.

The changes that occurred between the PGA and EGA scores during the study period were found to be significant \(( p < 0.001)\). Perceptions of improvement in disease activity showed the highest concordance. Patients who were perceived to have improved had the highest baseline PGA and EGA scores. They also had the biggest changes in the pain score and the number of swollen joints and tender joints. Where patients and clinicians perceived that the disease activity had worsened, the concordance was lower. The pain score, the number of swollen joints and the number of tender joints appeared to be the main determinants of the changes seen in the PGA and EGA scores \(( \Delta r^2 = 0.346, \Delta r^2 = 0.125 \) and \( \Delta r^2 = 0.036 \) respectively). Overall, the study found that pain appears to be the most important determinant of a patient’s perceptions of disease activity. The most important determinant of disease activity for clinicians appeared to be the number of swollen joints. A multivariate analysis of the data suggests that patients assess their disease activity as worse than physicians do.
The authors emphasise the importance of understanding the patient’s priorities for management when making treatment decisions because the problems they face may not be a direct result of joint disease. Co-existing conditions and chronic damage may also be an issue and this is particularly relevant for pain that is not caused by joint inflammation. Reducing non-inflammatory pain may help to increase concordance between patients’ and physicians’ assessments of disease activity and facilitate shared decision-making about the need for further treatments.\

Another study looking at the degree of discordance between clinicians’ and physicians’ assessments of the severity of disease found that 31% of patients differed from clinicians in their perceptions of disease severity. The authors used the visual analogue scale (VAS) to measure global disease severity and looked at:

- disease characteristics (rheumatoid factor, number of swollen and tender joints, ESR and DAS 28 score);
- functional status (measured using the HAQ); and
- symptoms of depression (measured using the Patient Health Questionnaire 9 (PHQ-9)).

The results showed:

- a positive discordance in 31% of the patient–physician dyads (patient–physician difference of >25 mm on the VAS);
- a negative discordance in 5% (less than -25 mm on the VAS);
- concordance in 64% (<25 mm on the VAS).

Symptoms of depression were an independent predictor of positive discordance (AOR 1.62, 95% CI 1.02–2.55). The authors hypothesise that the association between depression and discordance may be due to poor communication between the patient and clinician, but they recognise that further research is needed in this area.

The study also found a difference between mean scores for the Disease Activity Score (DAS) 28-4 variable and DAS 28-3 variable (which was calculated without the patient global assessment of disease severity) that was statistically significant (p = 0.001 for concordant groups, p < 0.001 for positive discordant groups and p = 0.007 for negative discordant groups). Patients with positive discordance had a mean DAS 28-3 score that was on average 0.54 lower compared to concordant patients whose score was an average of 0.08 lower.

These differences suggest that DAS 28 score may not be an accurate reflection of the activity of disease in patients with positive discordance.

The association between depression and discordance may have an effect on DAS 28 scores. DAS 28 scores that indicate moderate to high disease activity may result in clinicians starting more intensive treatment when the patient’s disease activity could potentially be more influenced by symptoms of depression rather than any joint pain or swelling. Alternatively, there may be a mechanism whereby depression itself affects the efficacy of treatment so that the perception of response to treatment is not as great as it otherwise would be (which would be reflected in the DAS 28 score).

Evidence has shown that depression may affect a patient’s response to treatment and the way in which they report symptoms. A study looking at the prevalence of depression in 159 patients starting treatment with anti-TNF drugs found that 47.5% of patients were depressed at baseline. The percentage of patients who remained depressed (but continued with treatment) fell to 15% at 12 months. Five patients were diagnosed with depression over the study period. Patients who were depressed at baseline had higher DAS 28 scores than those who were not depressed but this difference was not statistically significant at 12 months (p = 0.42). Treatment with anti-TNF therapy appeared to have less effect on disease activity in patients with persistent depression compared to patients who were not depressed. At three months, patients with persistent depression had a lower reduction in the DAS 28 score than people who did not have depression (median (interquartile range) change DAS 28 1.71 (0–2.6) vs 2.2 (1.5–3.2) p = 0.005). An explanation for this might be the effect that symptoms of depression have on the objective and subjective measures of inflammation. For example, the 28-swollen-joint-count at three months in depressed patients was 7 compared to 4 in patients who did not have depression (p = 0.006). The 28-tender-joint-count at three months was 9 in depressed patients compared to 5 for patients without depression (p = 0.001). These findings suggest that patients with depression, particularly those with persistent symptoms, do not respond as well to treatment with anti-TNF therapy. Managing depression in these patients may help to improve the effectiveness of treatment.

Further studies are needed to examine the effect of discordance on the assessment of disease activity (particularly on the DAS 28 scores) and to look at the effect of depression on communication between patients and healthcare providers.

Factors to consider when using patient-reported outcomes

Patient-reported outcomes (PROs) are useful because they provide information about the patient’s perspective on aspects of their disease. Measurement of objective outcomes, such as pain and fatigue, are seen as important by patients and so it would follow that these outcomes should be reported by patients themselves. Patient-reported outcome measures that assess functional limitations and symptoms are of most interest clinically because they are indicative of the severity of a disease and provide information about the response to treatments. Discordance between patients’ and clinicians’ assessments of disease activity may have an adverse effect on treatment decisions, but an argument has been made that, in some instances, discordance could help to guide treatment decisions. For example, if a patient is experiencing a lot of symptoms but there is no evidence of inflammation this could lead to a decision to make changes in treatments that modify symptoms rather than making changes to any disease-modifying treatments. There are challenges with using some PROs to assess the efficacy of treatments because the link between them and the pathophysiology and treatment of rheumatoid arthritis is not clear. Further research is needed to establish how useful PROs are at predicting long-term outcomes and how to approach discordance when making treatment decisions.
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References


