EXTENDED REPORT

The comparative effectiveness of anti-TNF therapy and methotrexate in patients with psoriatic arthritis: 6 month results from a longitudinal, observational, multicentre study

M S Heiberg, C Kaufmann, E Rødevand, K Mikkelsen, W Koldingsnes, P Mowinckel, T K Kvien

Ann Rheum Dis 2007;**66**:1038–1042. doi: 10.1136/ard.2006.064808

See end of article for authors' affiliations

Correspondence to:
Dr Marte Schrumpf Heiberg,
Dept. of Rheumatology,
Diakonhjemmet Hospital,
Box 23 Vinderen, 0319
Oslo, Norway; marte.schrumpf@diakonsyk.no

Accepted 21 December 2006
Published Online First
9 January 2007

Objectives: To compare the response to treatment with tumour necrosis factor (TNF) inhibitors and methotrexate (MTX) monotherapy in patients with psoriatic arthritis (PsA) within a real-life clinical setting.

Methods: We analysed data from an ongoing longitudinal, observational multicentre study in Norway. Our data comprised 526 cases of patients with PsA who received either anti-TNF treatment (n=146) or MTX monotherapy (n=380) and were followed for at least 6 months with measures of disease activity, health status and utility scores. A propensity score was computed to adjust for channelling bias. The changes in measures of disease activity and health-related quality of life from baseline to 3- and 6-month follow-up were compared between the groups with adjustments for the baseline value of the dependent variable and the propensity score (analyses of covariance (ANCOVA)).

Results: The groups were significantly different at baseline with respect to demographic and disease activity measures. The variables included in the propensity score were age, sex, number of previous disease modifying anti-rheumatic drugs (DMARDs), presence of erosive disease, treatment centre and investigator's global assessment. The adjusted changes at 6 months were significantly larger in the anti-TNF group for ESR, DAS-28, M-HAQ, patient's assessments of pain, fatigue and global disease activity on a visual analogue scale (VAS) and 4 out of 8 SF-36 dimensions.

Conclusions: Clinical improvement was superior with TNF inhibitors compared to MTX monotherapy in patients with PsA, when assessed in this setting of daily clinical practice.

Psoriatic arthritis (PsA) is an inflammatory arthropathy that affects about 0.2–1% of the population.^{1,2} The recent introduction of new, effective treatment options has resulted in renewed interest in PsA and other seronegative spondyloarthritides. Tumour necrosis factor (TNF) inhibiting agents have been shown to be effective in PsA in several randomised controlled trials (RCTs).^{3–5} However, conventional disease modifying anti-rheumatic drugs (DMARDs) are still the first choice of therapy, although the documentation of efficacy is scarce for these drugs.⁶ Methotrexate (MTX) is probably the most extensively used DMARD in PsA² but the efficacy is only documented through two small RCTs.^{7,8} Thus, there is a need for further systematic evaluation of the efficacy of the traditional DMARDs, and to compare them with the more expensive biological drugs.

RCT is the gold standard for clinical trials. However, strict inclusion criteria and short duration of the trials limit the external validity of results from RCTs.^{9,10} Effectiveness refers to how well a drug performs under real-life conditions outside the context of a randomised trial.¹¹ Longitudinal, observational study is the preferred design for studying effectiveness.¹¹ A register of DMARD prescriptions (including biological therapy) for patients with inflammatory arthropathies has been established in Norway¹² and provides an opportunity to compare effectiveness across treatment regimens in a real-life setting. The aim of this analysis was to compare the effectiveness of TNF-blocking therapy and MTX monotherapy in patients with PsA.

MATERIALS AND METHODS

Setting

The Norwegian DMARD (NOR-DMARD) register was established in December 2000. Five Norwegian Rheumatology

Departments consecutively include all patients with inflammatory arthropathies, starting with a DMARD regimen. Patients are registered as a new case when they switch to another DMARD regimen, which also includes, for example, adding a TNF antagonist to MTX monotherapy. The study design is a phase IV, multicentre, longitudinal, observational study. Demographic variables are recorded at baseline and patients are assessed at baseline, after 3, 6 and 12 months, and then yearly with core measures of disease activity and health status measures. We managed to include about 85% of the patients who start with DMARD therapy. The remaining 15% were either missing, refused enrolment, or were excluded due to language barriers, inclusion in RCTs etc. By January 2006, 5276 cases were enrolled in the NOR-DMARD register.

Patients

Patients were eligible for inclusion in the present analyses if they had been diagnosed with PsA by the treating rheumatologist (i.e. they were given the diagnoses L40.5+M07.0, M07.2 or M07.3 according to the WHO international classification of diseases (ICD-10)), received either methotrexate monotherapy or TNF-blocking agents and had been included in the register for at least 6 months (fig 1). The eligibility criteria were met in 526 cases. Mean (SD) age of the patients was 48.1 (12.7) years, disease duration 7.4 (8.2) years, 47.3% were females and 34.7% had erosive disease. A total of 380 patients received methotrexate monotherapy (mean (SD) dose 10.2 (3.2) mg weekly) and 146 patients received TNF-blocking agents (44 infliximab, 83 etanercept and 19 adalimumab, of these 75%, 60% and 79%, respectively, with concomitant MTX (mean (SD) dose 12.5 (4.7) mg weekly)). Data for the 6-month LOCF analyses was not available for 24 (6.3%) of the patients in the MTX group and 14 (9.6%) of the patients in the anti-TNF group. The most

common dosing regimen for infliximab was 3–5 mg/kg at baseline, after 2 and 6 weeks and then every eighth week, for etanercept 25 mg twice weekly, and for adalimumab 40 mg every second week. A total of 108 (74%) of the patients in the anti-TNF group had previously used MTX, and 39 of these patients were previously included in the MTX group. The patients gave written informed consent before participation. The study was approved by the regional ethical committee, and the storage of data was approved by the Data Inspectorate.

Assessments

Patients were assessed at baseline and after 3 and 6 months with measures of disease activity and health status that are applicable in rheumatoid arthritis but also in other inflammatory arthropathies. The 28-joint counts were performed partly by rheumatologists and partly by trained study nurses. The disease activity score-28 (DAS-28) was computed based on 28 tender and swollen joint counts, patient’s global assessment on a 100 mm visual analogue scale (VAS) and the erythrocyte sedimentation rate (ESR). Different variants of DAS, including DAS-28, have been shown to be discriminant and responsive in PsA.¹³ The treating rheumatologist filled in the information about rheumatoid factor status and erosive disease, i.e. whether it was present or not present. The health assessment questionnaire (HAQ)¹⁴ measures physical function and is commonly used in clinical trials of PsA.¹⁵ M-HAQ is a shortened, modified version of HAQ with a score from 1 to 4 (where 4 = worst disability).¹⁶ The Medical Outcome Study 36-item short form health survey (SF-36)¹⁷ is a commonly used health status measure. It contains 36 questions measuring health across eight different dimensions: physical functioning, role limitations due to physical health problems, bodily pain, vitality, social functioning, role limitations due to emotional problems, mental health and general health. A score is computed within each dimension with a value from 0 (worst possible health state) to 100 (best possible health state). Short form-6D (SF-6D) is a utility score, based on SF-36, and was computed according to a published algorithm.¹⁸ The score ranges from 0 (dead) to 1 (perfect health). All treatment terminations were registered.

Analyses

Baseline values were compared using two-sample t-tests (continuous variables) and chi-square tests (categorical variables). Within-group changes from baseline to the 3-and 6-month follow-up assessments were examined by paired samples t-test, and group differences were assessed using analyses of covariance (ANCOVA)¹⁹ with adjustments for the baseline value and the propensity score. The propensity score reflects the propensity for receiving anti-TNF versus methotrexate therapy²⁰ and was computed in order to statistically adjust for confounding by indication. Potential variables for inclusion in the propensity score (age, gender, disease duration, number of previous DMARDs, presence of erosive disease, ESR, CRP, patient’s assessment of joint pain (VAS), patient’s assessment of fatigue (VAS), patient’s global assessment of health (VAS), investigator’s global assessment (VAS), M-HAQ score DAS-28, SF-6D) were explored in univariate analyses with a p-level of 0.25 as the cut-off for inclusion in the model. Further selection of variables that predicted the choice of therapy was made according to statistical significance in a logistic regression analysis. The groups were balanced with respect to age and gender by including these variables in the propensity score regardless of statistical significance. Variables included in the final model were age, gender, investigator’s global assessment, number of previous DMARDs, erosive disease and treatment centre. A comparative subanalysis was performed between patients receiving anti-TNF monotherapy and anti-TNF in combination with MTX. The crude drug-adherence rates were explored in a Kaplan–Meier analysis, and the risk ratio (RR) for treatment withdrawal was assessed with adjustment for the propensity score in a Cox regression analysis. All changes were examined with a last observations carried forward (LOCF) approach when values were missing, with at least one follow-up examination being required. A significance level of 5% was used in all the analyses. No correction for multiple comparisons was performed. Statistical analyses were performed with SPSS software, V.12.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Group characteristics and baseline values are shown in table 1.

Figure 1 Selection of patients from the NOR-DMARD register for the present analyses. PSA, psoriatic arthritis; RA, rheumatoid arthritis; AS, ankylosing spondylitis; JA, juvenile arthritis; DMARD, disease modifying anti-rheumatic drug; MTX, methotrexate; TNF, tumour necrosis factor.

Table 1 Baseline demographic and disease variables in the two treatment groups

	Methotrexate (n = 384)	Anti-TNF (n = 147)	p-Value
Age	48.9 (13.2)	46.0 (11.1)	0.01
Females	49.7	40.8	0.07
Disease duration, years	5.8 (7.2)	11.6 (9.3)	<0.001
No. of previous DMARDs	0.5 (0.8)	2.6 (1.7)	<0.001
Erosive disease	27.8	56.3	<0.001
Rheumatoid factor positive	5.9	6.4	0.83
Investigator's global assessment	35.0 (15.2)	44.8 (19.6)	<0.001

Values are presented as mean (standard deviation of the mean) for continuous variables and as % for categorical variables. DMARDs, disease modifying anti-rheumatic drugs.

Patients receiving anti-TNF treatment had generally more active and severe disease than patients in the MTX group.

The TNF group had significantly worse health related quality of life (HRQoL) across all SF-36 dimensions compared to MTX at baseline, except for the two dimensions comprising mental health (table 2).

Except for VAS fatigue and SF-36 general health in the MTX group, significant improvement from baseline was seen for all measures in both treatment groups at 3 and 6 months (results not shown). Comparison of the crude changes revealed statistically significant differences in favour of the TNF group for most of the measures except for the swollen joint counts and SF-36 role mental (results not shown).

The mean propensity score in the two treatment groups were 0.13 (MTX) and 0.65 (anti-TNF). After adjusting for the propensity score and the baseline value of the dependent variable, the between-group differences were significantly in favour of the anti-TNF group for ESR, the patient's assessment of joint pain, fatigue and global health, DAS-28, M-HAQ and 4 SF-36 domains (bodily pain, vitality, role physical and general health) at 3 and 6 months (table 2). The different improvement in SF-36 resulted in a comparable, or even a slightly better level of HRQoL after 6 months in anti-TNF group compared to the

MTX group. The change in SF-6D score was borderline significant in favour of TNF inhibitors (table 2).

In the anti-TNF group, baseline values and changes from baseline were similar across the subgroups of patients who did and did not receive concomitant MTX (results not shown). After 6 months, the drug adherence rates in the MTX group and the anti-TNF group were 82.9% and 81.4%, respectively. The risk of terminating the treatment within the first 6 months was similar in the two groups, also after adjusting for the propensity score. The main reason for treatment terminations in both groups was adverse events, causing 52.4% of treatment terminations in the MTX group and 77.8% of the treatment terminations in the anti-TNF group. The adverse events are listed in table 3.

DISCUSSION

The introduction of biological drugs represents a major progress in the treatment of psoriatic arthritis, and has led to an increased interest in the disease. The efficacy of TNF-blocking agents has been demonstrated through several randomised

Table 3 Adverse events reported by the patients that were the reason for their withdrawal from treatment

	Methotrexate (n = 34)	Anti-TNF (n = 21)
Nausea	12	4
Elevated liver enzymes	7	4
Stomatitis	5	5
Diarrhea	6	0
Exanthema	5	1
Respiratory tract infection	1	5
Cough/dyspnoea	2	3
Fever/"influenza"	1	3
Headache	4	0
Injection site reaction	0	2
Trombocytopenia	0	1
Allergic reaction	0	1
Urinary tract infection	0	1
Other	4	4

Table 2 Clinical variables at baseline and 6-month changes (estimated marginal means) after adjustments for the baseline value and the propensity score

	Baseline			6-month changes		
	MTX (n = 380)	Anti-TNF (n = 146)	p-value*	MTX (n = 356)	Anti-TNF (n = 132)	p Value*
ESR	23.6 (20.1)	30.4 (28.1)	0.01	-6.7 (14.4)	-16.3 (12.5)	<0.001
SJC	4.9 (4.4)	4.9 (4.8)	0.97	-2.1 (3.3)	-2.1 (3.8)	0.91
TJC	6.3 (5.6)	7.5 (7.0)	0.08	-2.3 (3.1)	-2.7 (6.2)	0.57
VAS fatigue	46.7 (28.5)	56.8 (25.3)	<0.001	-0.4 (27.3)	-12.7 (32.1)	0.001
VAS pain	48.3 (22.0)	53.5 (22.4)	0.02	-9.6 (23.3)	-21.6 (27.4)	<0.001
VAS patient's global	52.2 (21.0)	58.1 (21.3)	<0.01	-11.6 (23.2)	-22.7 (27.3)	<0.001
DAS-28	4.5 (1.2)	4.8 (1.4)	0.02	-0.8 (1.3)	-1.7 (1.6)	<0.001
M-HAQ	1.64 (0.45)	1.83 (0.47)	<0.001	-0.16 (0.4)	-0.30 (0.5)	0.01
SF-36:						
Physical function	53.0 (22.8)	42.3 (21.6)	<0.001	6.8(21.8)	12.3(25.7)	0.06
Role (physical)	21.6 (32.5)	12.5 (25.3)	0.001	11.9(38.9)	25.6(45.8)	0.01
Bodily pain	32.9 (16.5)	29.1 (17.0)	0.02	10.2(20.1)	17.8(23.6)	0.01
General health	50.3 (20.3)	40.0 (16.8)	<0.001	2.0(19.4)	7.0(22.8)	0.03
Vitality	40.6 (22.4)	30.8 (20.0)	<0.001	5.2(20.7)	12.0(24.3)	0.01
Social function	65.3 (26.3)	56.7 (24.2)	0.001	7.1(23.6)	9.0(27.8)	0.56
Role (mental)	50.8 (42.2)	52.2 (43.8)	0.74	10.0(40.0)	9.9(47.0)	0.98
Mental health	71.2 (18.6)	70.0 (18.0)	0.39	2.6(15.2)	4.7(17.8)	0.30
SF-6D	0.57 (0.10)	0.55 (0.09)	<0.01	0.040 (0.10)	0.066 (0.11)	0.07

Values are presented as mean (standard deviation of the mean). ESR, erythrocyte sedimentation rate; SJC, Swollen joint count (28 joints); TJC, tender joint count (28 joints); VAS, visual analogue scale; DAS, disease activity score; M-HAQ, modified health assessment questionnaire; SF-6D, short form 6D.

*p-value for anti-TNF compared to MTX.

controlled trials.^{3–5} The efficacy of traditional DMARDs, by contrast, is poorly documented through systematic trials.⁶ Nevertheless, they are widely used, mainly based on the clinical impression that these drugs are effective. Systematic studies that explore the efficacy of traditional DMARDs in PsA, as well as the comparative efficacy between traditional DMARDs and biological treatments are in demand. In the present longitudinal observational study we compared the real-life performance of MTX and TNF-inhibitors in patients with PsA. Patients in both treatment groups in the present study improved, but the improvement was larger with TNF-inhibitors compared to MTX (table 2).

Although the preferred design for studies addressing comparative efficacy is RCT, longitudinal observational studies can provide additional information of value as they are conducted in a patient population treated in a real-life clinical setting. However, several biases complicate the analyses and interpretation of the results. One obvious limitation is the lack of randomisation and confounding by indication, which is one of the major challenges in observational studies, as treatment decisions depend on the condition of the patient at the time of inclusion. Propensity modelling is the contemporary method for statistical “semi-randomisation”.²⁰ The aim of the method is to identify important factors that predict the treatment decisions and then balance the groups with respect to these factors. Another challenge in observational studies is missing data. Data for the 6 month LOCF analyses was not available in 24 (6.3%) of the patients in the MTX group and 14 (9.6%) of the patients in the anti-TNF group. A total of 108 (74%) of the patients in the anti-TNF group had previously used MTX, and 39 of these patients were also included in the MTX group. However, when excluding the patients represented in both groups from the analyses, the results remained similar. Interestingly, the mean age in the TNF group was lower than the mean age in the MTX group, whereas disease duration was significantly longer. This might indicate a bias against using biological therapy in older persons.

The anti-TNF group in our study comprises all patients using infliximab, etanercept and adalimumab, with or without concomitant MTX. We performed a subanalysis comparing the anti-TNF monotherapy with the combination with MTX. These groups were similar with regard to baseline scores and changes from baseline, justifying that they were considered as one group. The finding corresponds with results from RCTs.^{4–5–21} Although no head-to-head comparisons have been performed between the different TNF-blocking agents, similar magnitude of clinical response has been observed across trials with the different agents with respect to joint symptoms, whereas improvements in skin manifestations seem to be somewhat greater with the monoclonal antibodies.^{4–5–21} Only two minor RCTs with MTX for PsA have been conducted.^{7–8} In 21 PsA patients, of whom 10 received parenteral MTX, significant improvements in skin and joint symptoms were observed in the MTX group compared to the placebo group.⁷ The other placebo-controlled trial with 37 patients failed to demonstrate superiority of orally administered MTX versus placebo for other measures than physician assessment of arthritis activity.⁸ In our study, the MTX group improved significantly from baseline for nearly all measures, although these results cannot be considered as any proof of the efficacy of MTX in PsA as a control group with placebo or a potentially less effective DMARD was not included.

Development and validation of assessment tools, as well as diagnostic and classification criteria, in PsA, is the focus of several initiatives lately.¹⁵ At the time of writing, no core set of assessments has yet been agreed upon. The limited joint count (28 joints) is a potential weakness in our study. Experts have

different opinions with respect to the number of joints to be counted, but the composite measure DAS-28 has been shown to be discriminant and responsive in placebo-controlled clinical trials, whereas the 28 swollen- and tender joint counts per se showed less discriminative ability than more extensive joint counts.¹³ This is in accordance with the findings in our study, where the 28-joint counts did not reveal differences between the groups, whereas the composite measure, DAS-28, was significantly different at baseline and with regard to change. Several trials have demonstrated improved health related quality of life (HRQoL) in PsA treated with TNF-blocking agents.^{4–5–22} In the IMPACT 2 trial²² the improvements in the 8 SF-36 scores were comparable to the changes in the anti-TNF-group in the present study. Our study also showed that anti-TNF treatment was superior to MTX in improving bodily pain, vitality, role physical and general health scores.

The cost-effectiveness of etanercept compared to ciclosporin and leflunomide in PsA patients was recently explored by Bansback *et al.*²³ They demonstrated, by modelling treatment over 10 years, that 0.82 and 0.65 more quality adjusted life years (QUALYs) were gained with etanercept as compared to ciclosporin and leflunomide, respectively, using the utility measure EQ-5D. The utility measure SF-6D, computed from the SF-36 items, is used in NOR-DMARD. We found that the 6-month improvement in SF-6D was 0.066 in the anti-TNF group and 0.040 in the MTX group, with a between group difference of 0.026 QUALYs. These results are, however, not directly comparable as EQ-5D usually results in a larger gain in QUALYs than SF-6D due to different floor and ceiling effects of these instruments.²⁴

A full set of domains to be assessed would ideally include skin involvement, dactylitis, enthesitis, spine involvement and radiological outcome. For feasibility reasons these assessments are not incorporated in the NOR-DMARD register, thus all patients, irrespective of type of inflammatory arthropathy, are assessed by the same set of assessment tools. It appeared that individual core measures of disease activity for RA, the composite measure DAS-28 as well as measures of HRQoL, differentiated between anti-TNF drugs and MTX. For exploratory purposes we also looked at two recently developed composite measures for RA, the simplified disease activity index (CDAI)²⁵ and the clinical disease activity index (SDAI (=CDAI + C-reactive protein)).²⁶ In this setting SDAI discriminated between the two treatment groups, whereas CDAI did not.

The diagnoses were made by the treating rheumatologists. About 6% of the patients were positive for rheumatoid factor (RF), and we cannot exclude that some of these patients had rheumatoid arthritis plus psoriasis. However, the percentage of RF positive patients was similar in the two groups.

The efficacy of TNF inhibitors in patients with PsA have been thoroughly explored in placebo-controlled RCTs. This longitudinal observational study is to our knowledge the first study in which the comparative effectiveness of TNF inhibitors and MTX is assessed. Our conclusion is that PsA patients seem to benefit more from TNF-blocking agents than MTX when treated in daily clinical practice. This result is consistent with findings in RCTs and contributes to improve external validity of results from RCTs examining anti-TNF drugs in PsA. However, more studies are needed to further establish the role of traditional DMARDs in the treatment of PsA.

Authors' affiliations

M S Heiberg, P Mowinckel, T K Kvien, Dept. of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

C Kaufmann, Dept. of Rheumatology, Buskerud Central Hospital, Drammen, Norway

E Rødevand, Dept. of Rheumatology, St. Olav Hospital, Trondheim, Norway

K Mikkelsen, Dept. of Rheumatology, Lillehammer Hospital for Rheumatic Diseases, Lillehammer, Norway

W Koldingsnes, Dept. of Rheumatology, University Hospital Northern Norway, Tromsø, Norway

Research grants for the NOR-DMARD study have been received from Abbott, Amgen, Wyeth, Aventis, MSD, Schering-Plough/Centocor and the Norwegian Directorate for Health and Social affairs. This work was supported by The Norwegian Women's Public Health Association.

Competing interests: MSH has received honoraria as a speaker and consultant from Abbott and Wyeth. CK reports no conflicts of interest. ER has received investigator honoraria from Abbott. KM has received speaker honoraria from Abbott. WK has received speaker honoraria from different pharmaceutical companies, including Wyeth and Schering-Plough. PM reports no conflicts of interest. TKK has received research grants and honoraria as a speaker and consultant from several pharmaceutical companies, including Abbott, Schering-Plough and Wyeth.

REFERENCES

- Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;**64**(Suppl 2):ii14-17.
- Madland TM, Apalset EM, Johannessen AE, Rossebo B, Brun JG. Prevalence, disease manifestations, and treatment of psoriatic arthritis in western Norway. *J Rheumatol* 2005;**32**(10):1918-22.
- Antoni CE, Kavanaugh A, Kirkham B, Tutuncu Z, Burmester GR, Schneider U, et al. Sustained benefits of infliximab therapy for dermatologic and articular manifestations of psoriatic arthritis: results from the infliximab multinational psoriatic arthritis controlled trial (IMPACT). *Arthritis Rheum* 2005;**52**(4):1227-36.
- Mease PJ, Kivitz AJ, Burch FX, Siegel EL, Cohen SB, Ory P, et al. Etanercept treatment of psoriatic arthritis: safety, efficacy, and effect on disease progression. *Arthritis Rheum* 2004;**50**(7):2264-72.
- Mease PJ, Gladman DD, Ritchlin CT, Ruderman EM, Steinfeld SD, Choy EH, et al. Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2005;**52**(10):3279-89.
- Nash P, Clegg DO. Psoriatic arthritis therapy: NSAIDs and traditional DMARDs. *Ann Rheum Dis* 2005;**64**(Suppl 2):ii74-7.
- Black RL, O'Brien WM, Vanscott EJ, Auerbach R, Eisen AZ, Bunim JJ. Methotrexate therapy in psoriatic arthritis: double-blind study on 21 patients. *JAMA* 1964;**189**:743-7.
- Willkens RF, Williams HJ, Ward JR, Egger MJ, Reading JC, Clements PJ, et al. Randomized, double-blind, placebo controlled trial of low-dose pulse methotrexate in psoriatic arthritis. *Arthritis Rheum* 1984;**27**(4):376-81.
- Kvien TK, Mikkelsen K, Nordvag BY. Results from controlled clinical trials: how relevant for clinical practice? *J Rheumatol* 2003;**30**(6):1135-7.
- Wolfe F, Michaud K, Dewitt EM. Why results of clinical trials and observational studies of antitumor necrosis factor (anti-TNF) therapy differ: methodological and interpretive issues. *Ann Rheum Dis* 2004;**63**(Suppl 2):ii13-7.
- Bombardier C, Maetzel A. Pharmacoeconomic evaluation of new treatments: efficacy versus effectiveness studies? *Ann Rheum Dis* 1999;**58**(Suppl 1):182-5.
- Kvien TK, Heiberg, Lie E, Kaufmann C, Mikkelsen K, Nordvag BY, et al. A Norwegian DMARD register: prescriptions of DMARDs and biological agents to patients with inflammatory rheumatic diseases. *Clin Exp Rheumatol* 2005;**23**(5)(Suppl 39):S188-94.
- Fransen J, Antoni C, Mease PJ, Uter W, Kavanaugh A, Kalden JR, et al. Performance of response criteria for assessing peripheral arthritis in patients with psoriatic arthritis: Analysis of data from randomized, controlled trials of two TNF inhibitors. *Ann Rheum Dis*. Published Online First: 27 April 2006, doi:10.1136/ard.2006.051706.
- Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: Dimensions and Practical Applications. *Health Qual Life Outcomes* 2003;**1**(1):20.
- Gladman DD, Mease PJ, Krueger G, van der Heijde DM, Antoni C, Helliwell PS, et al. Outcome measures in psoriatic arthritis. *J Rheumatol* 2005;**32**(11):2262-9.
- Pincus T, Summey JA, Soraci SA Jr, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. *Arthritis Rheum* 1983;**26**(11):1346-53.
- McHorney CA, Ware JE Jr, Lu JF, Sherbourne CD. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med Care* 1994;**32**(1):40-66.
- Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. *J Health Econ* 2002;**21**(2):271-92.
- Kleinbaum DG. *Applied regression analysis and other multivariable methods*. Boston: PWS-Kent Publishing Company, 1988.
- Austin PC, Grootendorst P, Anderson GM. A comparison of the ability of different propensity score models to balance measured variables between treated and untreated subjects: a Monte Carlo study. *Statist Med*. Published Online First: 17 May 2006, doi:10.1002/sim.2580.
- Antoni C, Krueger GG, de Vlam K, Birbara C, Beutler A, Guzzo C, et al. Infliximab improves signs and symptoms of psoriatic arthritis: results of the IMPACT 2 trial. *Ann Rheum Dis* 2005;**64**(8):1150-7.
- Kavanaugh A, Antoni C, Krueger GG, Yan S, Bala M, Dooley LT, et al. Infliximab improves health related quality of life and physical function in patients with psoriatic arthritis. *Ann Rheum Dis* 2006;**65**(4):471-7.
- Bansback NJ, Ara R, Barkham N, Brennan A, Fraser AD, Conway P, et al. Estimating the cost and health status consequences of treatment with TNF antagonists in patients with psoriatic arthritis. *Rheumatology (Oxford)* 2006;**45**(8):1029-38.
- Brazier J, Roberts J, Tsuchiya A, Busschbach J. A comparison of the EQ-5D and SF-6D across seven patient groups. *Health Econ* 2004;**13**(9):873-84.
- Aletaha D, Nell VP, Stamm T, Uffmann M, Pflugbeil S, Machold K, et al. Acute phase reactants add little to composite disease activity indices for rheumatoid arthritis: validation of a clinical activity score. *Arthritis Res Ther* 2005;**7**(4):R796-R806.
- Smolen JS, Breedveld FC, Schiff MH, Kalden JR, Emery P, Eberl G, et al. A simplified disease activity index for rheumatoid arthritis for use in clinical practice. *Rheumatology (Oxford)* 2003;**42**(2):244-57.