

## EXTENDED REPORT

## Prognostic factors for remission in early rheumatoid arthritis: a multiparameter prospective study

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**Objective:** To determine prognostic factors for remission in early rheumatoid arthritis.

**Methods:** 191 patients with rheumatoid arthritis whose disease duration was less than one year were followed up prospectively for five years. Remission, defined by a disease activity score (DAS) of <1.6, was used as the outcome measure. Baseline clinical, laboratory, genetic, and radiographic data (with radiographic scores determined by Sharp's method, modified by van der Heijde) were obtained.

**Results:** 48 patients (25.1%) fulfilled the remission criteria at the three year follow up visit, and 30 (15.7%) at three and five years. On univariate analysis by Fisher's exact test, remission at three years and persistent remission at five years were closely correlated with baseline DAS values, C reactive protein level, Ritchie score, health assessment questionnaire score, duration of morning stiffness, and to a lesser extent baseline total radiological scores and rheumatoid factor negativity. No significant correlation was found with sex, age, extra-articular manifestations, erythrocyte sedimentation rate, anti-cyclic citrullinated protein antibodies, anti-keratin antibodies, anti-HSP 90, anticalpastatin antibodies, antinuclear antibodies, or HLA-DRB1\* genotypes. Logistic regression analysis showed that the baseline independent variables predictive of remission were low DAS, Ritchie score, morning stiffness duration, and total radiographic score.

**Conclusions:** Baseline prognostic factors for remission in early rheumatoid arthritis were mainly clinical markers of disease activity and radiological scores.

Rheumatoid arthritis is currently recognised as a heterogeneous entity that is usually diagnosed with reference to the American College of Rheumatology (ACR) classification criteria.<sup>1</sup> The clinical course of rheumatoid arthritis is variable and its prognosis is difficult to predict.<sup>2–3</sup> In many patients, the disease process is severe and results in progressive joint destruction and serious disability, but outcomes vary widely. Predicting the outcome of this disease is crucial for optimal clinical management. Patients with a high likelihood of an untoward outcome should be given appropriately aggressive treatment at an early stage; this is even more important now that new treatments have been shown to reduce progression of the disease.<sup>4–6</sup> The ultimate goal of treatment is remission—that is, complete suppression of disease activity.<sup>7</sup> The American Rheumatism Association (ARA) has defined preliminary remission criteria.<sup>8</sup> These criteria are based on six variables, of which two (fatigue and joint pain on motion) are not included in the core sets of variables uniformly collected in clinical studies.<sup>9</sup> Prevo *et al* proposed the disease activity score (DAS<sup>10</sup>) as a standardised evaluation tool to define remission, after showing in 227 patients that those with a DAS of <1.6 were in remission according to the ARA criteria.<sup>11</sup>

Remission is a pertinent outcome measure in rheumatoid arthritis, yet few studies have attempted to determine prognostic factors for remission. It has been claimed that if remission does occur, it tends to happen early; thus it is important to study patients in the early stages of the disease.

In the present prospective study, we investigated various clinical, laboratory, genetic, and radiographic indices in a cohort of patients with early rheumatoid arthritis. We evaluated remission rates (using the DAS) after three and five years of follow up and analysed prognostic factors for remission at three years, and for sustained three year and five year remission.

## METHODS

## Patients

Between March 1993 and October 1994, we recruited consecutive outpatients referred by primary care physicians for the purposes of the study from four French centres (Montpellier, Paris-Cochin, Toulouse, and Tours) who fulfilled the ACR criteria for rheumatoid arthritis,<sup>1</sup> had a disease duration of less than one year, and had not previously been treated with disease modifying antirheumatic drugs (DMARDs). All patients agreed to be enrolled in a five year follow up study and provided their signed informed consent. They were subsequently treated with DMARDs (usually methotrexate, sulphasalazine, or a combination of both), and the regimen could be modified during the study according to efficacy and tolerance.

The study was approved by the ethics review board in Montpellier.

## Clinical and biological assessment

The following evaluation data were collected at baseline: age; sex; body mass index; disease duration; duration of morning stiffness; patients' assessment of pain (on a visual analogue scale); number of swollen and tender joints; Ritchie articular index<sup>12</sup>; disease activity score; presence or absence of nodules and extra-articular manifestations; health assessment questionnaire (HAQ) score<sup>13</sup>; erythrocyte sedimentation rate (ESR); C reactive protein concentration; IgA and IgM rheumatoid factor (RF) positivity by anti-human Fc IgG enzyme linked immunosorbent assay (ELISA); antikeratin

**Abbreviations:** ACR, American College of Rheumatology; ARA, American Rheumatism Association, DAS, disease activity score; DMARD, disease modifying antirheumatic drug; HAQ, health assessment questionnaire

antibody positivity by indirect immunofluorescence on cryostat sections of rat oesophagus; anti-cyclic citrullinated protein (CCP) antibody positivity by ELISA<sup>14</sup>; antiperinuclear antibody positivity by immunofluorescence on buccal epithelial cells; anti-RA33 antibody positivity by immunoblotting<sup>15</sup>; anti-heat-shock protein 90 kDa antibody positivity by ELISA<sup>16</sup>; anticalpastatin antibody positivity by ELISA (Progen, Heidelberg, Germany); serum concentration of YKL-40 by radioimmunoassay (Chondrex Metra Biosystems, Mountain View, California, USA); and antinuclear antibody positivity by immunofluorescence on Hep-2 cells. HLA-DRB1 and DQB1 genotyping were done as previously described.<sup>17</sup> Each patient was followed up by the same investigator (BC, MD, PG, or AC) at six months after inclusion, at one year, and then after three and five years.<sup>17 18</sup>

### Radiographic assessment

Hand, wrist, and foot radiographs were obtained at baseline and at three and five years. They were evaluated blind and in chronological order by two independent observers and scored using Sharp's method as modified by van der Heijde.<sup>19</sup> For each patient, an erosions score, a joint space narrowing score, and a total damage score were noted for the hands and feet. The intraclass, intraobserver, and interobserver coefficients of correlation were calculated on 30 chosen pairs of radiographs of the hands and feet and were always greater than 0.85. No systematic differences were found in any of the scores. We then used the mean of the two observer scores to determine the final radiographic scores for erosions, joint space narrowing, and total damage.

### Outcome measurement

Remission was defined by a DAS of <1.6 at the three year follow up visit, according to Prevoo *et al.*<sup>11</sup> Persistent remission was defined by a DAS of <1.6 at the three year and five year evaluations.

### Statistical methods

Statistical analysis was done using BMDP statistical software.<sup>20</sup> The outcome variable was treated as a qualitative variable: the presence or absence of remission. Univariate analysis of the relation between all baseline values and the outcome measure was undertaken using the  $\chi^2$  test, with Yates' correction when appropriate, or Fisher's exact test. When these variables were continuous, they were transformed into categorical variables using the median value as the cut off point, except for ESR, where the cut off was chosen according to clinical experience (a cut off of 28 mm/hour). Odds ratios with 95% confidence intervals (CI) were estimated by the Mantel-Haenszel method.

A stepwise multiple logistic regression model was used to find relevant independent prognostic variables. The variables included in the multivariate model were selected using univariate analysis ( $p \leq 0.15$ ). The significance level was set at 0.05.

## RESULTS

### Demographic, clinical, and biological features of the patient cohort

The baseline characteristics of the patients are shown in table 1. We enrolled 191 patients in the study (140 women, 51 men). Their mean (SD) age at diagnosis was 50.5 (14.7) years and the mean disease duration at inclusion was 3.3 (2.6) months. Of these, 154 (80.6%) were IgM or IgA RF positive ( $\geq 20$  IU/ml and  $\geq 7$  units/ml, respectively) at baseline, and 86 (45%) had at least one rheumatoid arthritis associated DRB1\*04 allele (DRB1\*0401, 0404, 0405, or 0408). Six months after inclusion, 178 patients (93.2%) were taking DMARDs: 131 (68.6%) were taking one drug (58 methotrex-

**Table 1** Characteristics of 191 patients with rheumatoid arthritis

Sex, % women	73.3%
Age at diagnosis (years)	50.5 (14.7)
Duration of disease (months)	3.3 (2.6)
Morning stiffness (min)	84 (79.4)
Patient's assessment of pain (visual analogue scale) (mm)	57.5 (22.2)
Swollen joints (number)	9.0 (5.9)
Tender joints (number)	21 (10)
Ritchie score	17.5 (8.5)
HAQ score	1.3 (0.7)
DAS	4.1 (0.8)
Extra-articular manifestations (% patients)	8.4%
ESR (mm/h)	40.2 (28.5)
C reactive protein (mg/l)	34.1 (43.2)
RF positivity (% patients)	80.8%
IgM RF (%)	68.0%
IgA RF (%)	75.5%
Antibody positivity, % patients	
Anti-CCP	58.9%
Antiperinuclear	49.9%
Antikeratin	41.4%
Anticalpastatin	16.5%
Antinuclear	36%
Anti-HSP90	23.0%
Anti-RA33	27.2%
YKL40 serum concentration (ng/ml)	109.7 (79.9)
HLA-DRB1*04 (% patients)†	47.6%
HLA-DRB1*01 (% patients)	29.5%
Total Sharp score at baseline‡	3.6 (7.7)

Values are the mean (SD) unless stated otherwise.

Positive cut off values were as follows: IgM rheumatoid factor (RF),  $\geq 20$  IU/ml; IgA RF,  $\geq 7$  units/ml; antiperinuclear antibodies,  $\geq 1:20$ ; anti-cyclic citrullinated protein antibodies,  $\geq 50$  units/ml; antikeratin antibodies,  $\geq 1:80$ ; anticalpastatin antibodies,  $\geq 15$  units/ml; antinuclear antibodies,  $\geq 1:160$ .

Anti-CCP, anti-cyclic citrullinated protein; anti-HSP 90, anti-heat-shock protein 90 kDa antibodies; DAS, disease activity score; ESR, erythrocyte sedimentation rate; HAQ, health assessment questionnaire; RF, rheumatoid factor.

†DRB1\*04 includes DRB1\*0401, 0404, 0405, and 0408.

‡Total damage score on radiographic evaluation of the hands and feet.

ate, 59 sulphasalazine, 14 other DMARDs), and 47 (24.6%) a combination of methotrexate and sulphasalazine. During the five year follow up, a mean of 1.95 DMARDs (range one to five) were prescribed (methotrexate to 175 patients, sulphasalazine to 147, intramuscular gold to 41, hydroxychloroquine to 25, D-penicillamine to 14, cyclosporin to one). Eighty six patients received the same DMARD or the same combination of DMARDs during the five year follow up. Sixty three patients (33%) received a low dose of prednisone (5–15 mg/day) at least once during follow up.

### Remission rate

Fourteen patients (7.3%) were lost to follow up at three years. At five years, 26 patients (13.6%) were lost to follow up (six died, eight refused further follow up, 12 moved out of the area) and 31 (16.2%) had missing data at the five year evaluation and were excluded from the analysis. The baseline characteristics of these patients did not differ from those of the rest of the cohort except for higher antikeratin antibody positivity ( $p = 0.03$ ) in the patients with missing data.

Forty eight patients (25.1%) fulfilled the remission criteria at the three year follow up visit, 38 (19.9%) at the five year follow up visit, and 30 (15.7%) at both visits; 78.9% of patients in remission at three years were also in remission at five years (odds ratio 32.2,  $p < 0.00001$ ).

### Predictive variables identified by the univariate analysis

The results obtained by univariate analysis of the studied baseline variables are presented in table 2 for three year

**Table 2** Factors predictive of remission at three years

Baseline variable	p Value*	OR (95% CI)*
DAS <4	0.0009	3.2 (1.6 to 6.5)
HAQ score <1.25	0.0087	2.8 (1.3 to 6.4)
Ritchie score <17	0.019	2.29 (1.1 to 4.6)
C reactive protein <14.5 mg/l	0.041	2 (1.0 to 4.1)
Morning stiffness <60 min	0.051	2.1 (0.98 to 4.8)
Total Sharp score <4	0.053	1.99 (0.98 to 4.0)
Anti-HSP90 negativity	0.057	2.6 (0.94 to 7.3)
Erosion score =0	0.062	1.97 (0.95 to 4)
Tender joint count <21	0.069	2 (0.94 to 4.3)
Pain on visual analogue scale <59 mm	0.085	1.94 (0.9 to 4.1)
IgA RF negativity	0.14	1.75 (0.8 to 3.8)
No extra-articular manifestations	0.15	2.89 (0.6 to 13)
Anticalpastatin antibody negativity	0.18	0.54 (0.2 to 1.3)
IgM RF negativity	0.41	1.34 (0.65 to 2.8)
Swollen joint count <9	0.54	1.2 (0.6 to 2.5)
ESR <28 mm/h	0.77	1.1 (0.56 to 2.1)
Antikeratin antibody negativity	0.82	1.08 (0.5 to 2.2)
HLA-DRB1*01 negativity	0.81	0.91 (0.4 to 2.3)
HLA-DRB1*04 negativity†	0.88	0.95 (0.5 to 1.8)
Anti-CCP antibody negativity	0.95	1.02 (0.4 to 2.2)

\*Significance level calculated using the  $\chi^2$  with Yates' correction.

†DRB1\*04 includes \*0401, 0404, 0405, and 0408.

Anti-CCP, anti-cyclic citrullinated protein; CI, confidence interval; DAS, disease activity score; ESR, erythrocyte sedimentation rate; HAQ, health assessment questionnaire; OR, odds ratio; RF, rheumatoid factor.

remission. Baseline disease activity scores were the best predictive factors for remission. An initial DAS of <4 was the best predictor ( $p < 0.001$ ); an HAQ score <1.25, a Ritchie score <17, and a C reactive protein concentration of <14.5 mg/l were also significantly correlated with remission. Morning stiffness ( $p = 0.051$ ), total Sharp score ( $p = 0.053$ ), anti-HSP90 negativity ( $p = 0.057$ ), erosion score ( $p = 0.062$ ), and tender joint count ( $p = 0.069$ ) showed a trend towards association with remission. Univariate analysis of predictive factors for persistent three and five year remission is presented in table 3. A baseline DAS of <4, an HAQ score of <1.25, a Ritchie score of <17, a C reactive protein concentration of <14.5 mg/l, a total Sharp score of <4 points,

**Table 3** Predictive factors for persistent remission (DAS <1.6 at the three year and five year evaluations)

Baseline variable	p Value*	OR (95% CI)*
DAS <4	0.0003	4.8 (1.9 to 11.9)
C reactive protein <14.5 mg/l	0.010	3 (1.2 to 7.3)
Ritchie score <17	0.016	2.8 (1.2 to 6.8)
HAQ score <1.25	0.018	3.2 (1.1 to 8.9)
IgM RF negativity	0.02	2.6 (1.1 to 6.3)
Morning stiffness <60 min	0.04	2.7 (1.0 to 7.4)
Total Sharp score <4	0.04	2.3 (1.0 to 5.7)
Anti-HSP90 negativity	0.06	3.2 (0.9 to 11.4)
IgA RF negativity	0.10	2 (0.85 to 5.1)
Pain on visual analogue scale <59 mm	0.13	2 (0.8 to 5.0)
Antikeratin antibody negativity	0.16	1.94 (0.75 to 5.0)
Tender joint count <21	0.19	1.8 (0.7 to 4.6)
Anticalpastatin antibody negativity	0.29	0.58 (0.2 to 1.3)
Swollen joint count <9	0.51	1.3 (0.57 to 3.0)
ESR <28 mm/h	0.56	1.2 (0.5 to 2.9)
Anti-CCP antibody negativity	0.62	1.25 (0.5 to 4.7)
YKL40 negativity†	0.74	0.7 (0.07 to 6.3)
Erosion score =0	0.8	2.18 (0.9 to 5.3)
HLA-DRB1*01 negativity	0.8	0.89 (0.36 to 2.2)
HLA-DRB1*04 negativity‡	0.9	1.05 (0.5 to 2.4)

\*Significance level calculated using the  $\chi^2$  test with Yates' correction.

†Range 24–125 ng/ml.

‡DRB1\*04 includes \*0401, 0404, 0405, and 0408.

Anti-CCP, anti-cyclic citrullinated protein; CI, confidence interval; DAS, disease activity score; ESR, erythrocyte sedimentation rate; HAQ, health assessment questionnaire; OR, odds ratio; RF, rheumatoid factor.

duration of morning stiffness <60 minutes, and RF negativity were correlated with persistent three and five year remission. No association was noted for any other variable, including age, sex, antikeratin or anti-CCP antibody negativity, and rheumatoid arthritis associated HLA-DRB1 genes.

### Stepwise multiple logistic regression

Tables 4 and 5 give the entry parameters identified by the multivariate logistic regression models that were independently predictive of the presence of remission at three years, and of persistent remission at the three year and five year evaluations.

Low DAS, baseline total radiographic score, and Ritchie score were the most important factors determining remission both at three years and in the "sustained remission" analysis. A low HAQ score and short duration of morning stiffness were predictive of remission at three years. A low baseline C reactive protein concentration was predictive of persistent remission.

### DISCUSSION

This multiparameter prospective study of a cohort of out-patients with early rheumatoid arthritis (less than one year disease duration) identified predictive factors of three year remission and sustained three and five year remission. The outcome variable was remission as defined by a disease activity score of <1.6.<sup>11</sup> Univariate analysis tested most of the clinical, biological, immunological, and genetic factors previously reported as possible prognostic factors in rheumatoid arthritis. Analysis was done on baseline variables. Remission was correlated with low baseline DAS, HAQ score, Ritchie score, and C reactive protein concentration. Logistic regression analysis showed that the only independent variables that were significant predictors of both three year and sustained remission were low DAS, baseline total radiographic score, and Ritchie score.

The prevalence of remission is variable between studies, perhaps because there is still no universally accepted definition of remission. The preliminary ARA criteria<sup>8</sup> are not sufficiently precise, and are not all core measures in the follow up of patients with rheumatoid arthritis. Methods of patient referral and selection vary between studies, as well as the duration without symptoms used to define remission. All in all, comparisons between studies concerning remission rates are difficult. We evaluated remission as a dichotomous variable at one point in time: the three year follow up visit. We then evaluated how many of our patients were in remission both at the three year and the five year evaluation, and predictive factors of this "sustained" remission. The ARA preliminary criteria defined remission with a notion of time period (two months). This aspect was not investigated in the original study<sup>8</sup> or in the studies by Wolfe and Hawley<sup>21</sup> and Alarçon *et al.*<sup>22</sup> because their follow up was not standardised. The DAS was evaluated as a definition criterion for remission using a three month time period,<sup>11</sup> while Eberhardt and Fex used the ARA criteria but over a six month period.<sup>23</sup> Other studies looked at remission as a state at one point in time.<sup>21 22 24</sup>

We found that 25.1% of our patients were in remission after three years, 19.9% after five years, and 15.7% at both evaluations. Prevoo *et al* studied 227 patients with a median follow up of 3.9 years<sup>11</sup>; the percentage of patients with at least one visit fulfilling the ARA remission criteria was 25%; each year, 15% of the patients were in remission for at least two consecutive visits. Eberhardt and Fex<sup>23</sup> found that 20% of 183 patients achieved ARA defined remission periods of at least six months' duration; average length of remission was 20.5 months. In Wolfe and Hawley's study<sup>21</sup> of 458 patients with rheumatoid arthritis, with established disease and at

**Table 4** Stepwise logistic regression analysis of predictive factors of remission at three years

	Coefficient	SE	OR (95% CI)	p Value
<i>With DAS</i>				
Constant	-2.8	0.5	0	
DAS <4	1.75	0.4	5.7 (2.3 to 14.2)	<0.0001
Initial Sharp score <4*	1.05	0.4	2.9 (1.3 to 7.0)	0.017
Morning stiffness <60 min	1.91	0.5	2.5 (0.9 to 6.6)	0.056
<i>Without DAS</i>				
Constant	-0.79	0.4		
HAQ <1.25	0.83	0.4	2.3 (0.9 to 5.7)	0.06
Initial Sharp score <4*	1.06	0.4	2.9 (1.2 to 7.0)	0.01
Ritchie score <17	1.01	0.4	2.7 (1.1 to 6.7)	0.02
Morning stiffness <60 min	-0.82	0.5	2.3 (0.9 to 6.0)	0.08

\*Initial Sharp score was entered as categorical variable (0, low, 1, high); 4 is the median value of the total Sharp score at three years.

CI, confidence interval; DAS, disease activity score; HAQ, health assessment questionnaire; OR, odds ratio.

least three follow up visits, 18.1% fulfilled the ARA criteria once. In a French cohort, remission was obtained in 10.5% of patients, but in only 5% by the ARA criteria.<sup>25</sup> Our rate of remission is in the higher range of published results, perhaps because we used Prevoo's definition of remission, which may be less stringent than the ARA criteria. On the other hand, our patients presented with rheumatoid arthritis according to ACR criteria (while many other studies were done on patients with undifferentiated arthritis). Our patients were referred to tertiary care departments, often a criterion of severity; but in this study we asked primary care physicians to refer *all* their patients presenting with early arthritis, without selection on the basis of severity, so that theoretically our cohort reflects community based early rheumatoid arthritis severity. The highest cross sectional (one visit) rate of remission was found in a Finnish study,<sup>24</sup> where 27% of the patients were in ARA defined remission at the two year follow up and 32% at the six year follow up. That study involved 142 patients with early rheumatoid arthritis treated with DMARDs. Harrison *et al*,<sup>26</sup> in a community based rheumatoid arthritis cohort, found 19% in remission after two years, remission being defined as "no arthritis on examination and no DMARD or steroid treatment within the previous three months." Two other studies reported a cross sectional remission rate of around 7% after three and seven years, respectively.<sup>27, 28</sup> Both studies used "being symptom-free" as a definition of remission.

We found that clinical markers of disease activity were the main predictors of remission. Some other studies have attempted to identify factors measured close to disease onset that might be used to predict future remission. Recent

studies<sup>29, 30</sup> have like ours identified mainly clinical markers as predictive of remission. Eberhardt *et al* also identified a lower HAQ score as predictive.<sup>31</sup>

We found no association of sex or age with remission. In Wolfe and Hawley's study,<sup>21</sup> female sex, onset before the age of 60 years, and early development of erosions were associated with fewer remission periods. Harrison *et al* confirmed this finding of an association with sex but not age.<sup>26</sup> Like us, they found an association with less widespread joint involvement at baseline.

To our knowledge, we are the first to have looked at the correlation between radiographic scores and remission. In multivariate analysis, a baseline total Sharp score (as modified by van der Heijde) of less than 4 points was predictive of remission in our study. Conversely, in a prospective study Möttönen *et al* found that patients who having at least once remission had less radiological damage after six years, with the lowest progression of radiological damage in those in remission at both evaluation points (two years and six years).<sup>24</sup>

Other studies have reported that being RF negative is important for remission. In our work, RF status was correlated with persistent remission in univariate analysis (odds ratio 2.6). We found no predictive value of antikeratin or anti-CCP antibody negativity.

The influence of rheumatoid arthritis associated HLA-DRB1 alleles is controversial. Molenaar *et al*,<sup>32</sup> like us, found no association between remission (ARA criteria)<sup>8</sup> and HLA-DRB1 alleles or DR/DQ haplotypes in 167 patients. Similarly, Möttönen *et al* found that the presence of a shared epitope had no impact on remission rates in 165 patients.<sup>33</sup> Other workers found the opposite.<sup>34, 35</sup> In Eberhardt's prospective

**Table 5** Stepwise logistic regression analysis of predictive factors of persistent remission (DAS <1.6 at the three year and five year evaluations)

	Coefficient	SE	OR (95% CI)	p Value
<i>With DAS</i>				
Constant	-0.88	0.5		
DAS <4	1.7	0.6	5.5 (1.7-17.8)	<0.0001
Initial Sharp score <4*	1.07	0.5	2.7 (0.9-8.1)	0.02
C reactive protein <14.5 mg/l	0.9	0.5	2.5 (0.8-7.4)	0.09
<i>Without DAS</i>				
Constant	-1.03	0.5		
C reactive protein <14.5 mg/l	1.14	0.5	3.1 (1.0-9.0)	0.004
Ritchie score <17	1.4	0.6	4.2 (1.4-12.8)	0.012
Initial Sharp score <4*	1.01	0.5	2.7 (0.9-8.0)	0.05

\*Initial Sharp score was entered as categorical variable (0, low, 1, high).

CI, confidence interval; DAS, disease activity score; HAQ, health assessment questionnaire; OR, odds ratio.



study,<sup>23</sup> remission was more likely in seronegative patients having no shared epitopes or only a single one and fewer active joints at baseline.

The potential role of DMARD treatment was not evaluated in our study, because our cohort was DMARD-naïve at baseline, and then treated in a highly homogeneous way, mostly with methotrexate or sulphasalazine or both, prescribed less than six months after inclusion. This renders comparisons between subgroups irrelevant. Furthermore, clinical and radiological status was shown to be similar after 18 months of treatment with either methotrexate, sulphasalazine, or a combination of both,<sup>36</sup> making it unlikely that the different drug regimens could have induced different remission rates in our study. For Möttönen *et al*,<sup>37</sup> remission was predicted by treatment strategy: patients treated with a combination of DMARDs had a higher remission rate than those treated with monotherapy. The same investigators reported that a shorter delay before DMARD institution was predictive of remission for patients treated with a single DMARD, while this delay did not contribute to the induction of remission in those treated with combination DMARDs.<sup>38</sup> Verstappen *et al* recently confirmed similar remission rates but a shorter delay before first remission with more aggressive DMARDs.<sup>30</sup>

We did not study the implications of remission on disability and joint damage, but Eberhardt and Fex<sup>23</sup> found that outcome was worse for patients presenting with progressive rheumatoid arthritis than for those with a relapsing–remitting disease pattern; and Molenaar *et al* found that in patients with rheumatoid arthritis and inactive disease, functional disability is slight and most strongly associated with pain, joint damage, disease duration, and disease activity.<sup>39</sup> Thus remission appears to be a valuable outcome measurement in rheumatoid arthritis, with a clinical impact. However, in all the published studies, including ours, the factors identified are not strong enough to make accurate predictions of remission, even when used in combination.

In conclusion, prognostic factors for remission in early rheumatoid arthritis are mainly the baseline disease activity score, clinical markers of disease activity, and baseline radiological scores.

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