The Effect of Different Remission Definitions on Identification of Predictors of Both Point and Sustained Remission in Rheumatoid Arthritis Treated with Anti-TNF Therapy

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ABSTRACT. ***Objective.*** Predictors of remission in rheumatoid arthritis (RA) have been defined in cross-sectional analyses using the 28-joint Disease Activity Score (DAS28), but not with newer composite disease activity measures or using the more clinically relevant state of sustained remission. We have evaluated predictors of remission using cross-sectional and longitudinal durations of disease state, and by applying additional definitions of remission [American College of Rheumatology/European League Against Rheumatism Boolean, Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI)].

Methods. Individuals in the Alberta Biologics Pharmacosurveillance Program were classified for the presence of remission (point and/or sustained > 1 yr) by each of the 4 definitions. Multivariate models were constructed including all available variables in the dataset and refined to optimize model fit and predictive ability to calculate OR for remission.

Results. Nonsmoking status independently predicted point remission by all definitions (OR range 1.20–2.71). Minority ethnicity decreased odds of remission by DAS28 (OR 0.13) and CDAI (OR 0.09) definitions. Male sex was associated with DAS28 remission (OR 2.85), whereas higher baseline physician global (OR 0.67) and erythrocyte sedimentation rate values (OR 0.98) decreased odds of DAS28 remission. Higher baseline patient global score (OR 0.77) and swollen joint counts (OR 0.93) were negative predictors for CDAI remission. Higher baseline Health Assessment Questionnaire (OR 0.62) reduced odds for remission by the SDAI definition, and educational attainment increased these odds (OR 2.13). Sustained remission was negatively predicted by baseline physician global for the DAS28 (OR 0.80), and higher tender joint count (OR 0.96) for the CDAI.

Conclusion. We demonstrate the influence of duration of remission state and remission definition on defining independent predictors for remission in RA requiring anti-tumor necrosis factor therapy. These predictors offer improved applicability for modern rheumatology practice. (J Rheumatol First Release July 15 2014; doi:10.3899/jrheum.131451)

Key Indexing Terms:
RHEUMATOID ARTHRITIS REMISSION PREDICTORS OF RESPONSE

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Outcome measures in rheumatoid arthritis (RA) clinical trials and practice have evolved from relatively complex composite disease activity measures such as the American College of Rheumatology (ACR) response criteria[1] and the 28-joint Disease Activity Score (DAS28)[2] to simple Boolean or composite disease activity measures based on addition of core outcome domains. These include the ACR/EULAR (European League Against Rheumatism) Boolean definition of remission[3], the Simplified Disease Activity Index (SDAI)[4], and the Clinical Disease Activity Index (CDAI)[5]. Validated cutpoints for remission, the desirable disease activity state in RA, exist for each of these measures, and are useful for determining response to treatment in clinical trials and in day-to-day practice.

Past efforts to identify predictors for remission have largely been based on the ACR response criteria or the DAS28 definition of remission, as summarized by Katchamart, *et al* in a systematic review[6]. This review, which explicitly included only publications reporting on multivariate analyses, identified demographic factors (male sex, young age, late-onset RA, nonsmoker), disease presentation factors (short disease duration, low baseline disease activity, mild functional impairment, low baseline radiographic damage, seronegative status, low levels of acute-phase reactants), genetic and immune expression profiles, initial treatment approach (type and combination of therapeutic agents), and response factors that influence the odds of entering remission. These predictors are relevant in clinical practice because they are used to educate patients on their expected prognosis, and thereby guide treatment recommendations and inform the relevant risk-benefit profile of RA therapies and management strategies proposed.

The current literature lacks reports on the identification of predictive factors when newer definitions of remission are applied. It is repeatedly demonstrated that the DAS28 definition of remission (score < 2.6) is the least stringent of all the disease activity measures, and classifies about 3 times as many patients in remission as does the ACR/EULAR Boolean definition[7,8,9]. This means that the currently accepted predictors for remission perhaps include weak variables, and only the strongest predictors would emerge if the analysis considered more stringent definitions of remission. As well, many of the studies consider only a cross-sectional evaluation of remission, rather than a sustained state of disease activity. Sustained levels of remission are more beneficial for radiographic outcomes[10], and predictors of sustained remission will inform prognosis even further.

The objective of our study was to compare independent predictors of DAS28 remission to those identified when applying the ACR/EULAR Boolean, SDAI, and CDAI definitions of remission. We hypothesized that the strongest predictors would be associated with all definitions for remission. We also evaluated predictors based on a cross-sectional evaluation of remission compared to a longitudinal evaluation of disease activity status to define sustained remission.

MATERIALS AND METHODS

Data sources. The Alberta Biologics Pharmacosurveillance Program was initiated in 2004 to identify the efficacy, safety, and cost-effectiveness of new biologic therapies for RA[11]. Patients in Alberta qualify for biologic therapy cost coverage if they have RA refractory to parenteral methotrexate (MTX), in combination with at least 1 other disease-modifying antirheumatic drug (DMARD), and leflunomide. They must achieve and retain a minimum DAS28 improvement of 1.2 units and a minimum improvement of their Health Assessment Questionnaire (HAQ) score by 0.22 units over their baseline scores at 12 weeks to continue receiving cost coverage for therapy. Patients who fail to meet these response criteria will be switched to another agent. Patients participating in the program are assessed for disease activity, adverse events, effect on function and quality of life, healthcare use, and self-reported economic effect of their disease at the start of a new biologic agent, 12 weeks after initiation of that drug, and at 6-month intervals if no treatment switches have occurred. The patients are also brought in for assessment if they contact the program reporting suspected treatment failure or adverse events, which may require a treatment switch. This analysis was restricted to patients naive to biologic therapy (to reduce confounding introduced by prior response to biologic therapy in patients switching therapy) and who had at least 2 study visits. The study period for this analysis was April 2004 to March 2011.

Ethics. All patients provided informed consent in accordance with ethical standards described in the Declaration of Helsinki. The study is approved by the University of Calgary Health Research Ethics Board (E-20424) and by the University of Alberta Research Ethics Board (Study ID Pro00000914).

Outcomes. Clinical variables collected at study visits were used to determine achievement of the ACR/EULAR Boolean definition of remission, and to calculate disease activity scores for DAS28, SDAI, and CDAI. For each study visit, based on these scores and their recognized cutpoints for remission (< 2.6, < 3.3, and < 2.8, respectively), subjects were categorized as being in remission or not for each separate definition at any single visit (point remission). We also used an ACR Boolean definition excluding the acute-phase response result, as Kuriya, *et al*, have done[9], in sensitivity analysis. Longitudinal disease course was considered to classify patients for sustained remission, defined as patients classified in remission on at least 2 consecutive visits with no treatment changes and no steroid requirements for a minimum of 1 year.

Covariates. We included disease duration at first anti-tumor necrosis factor (TNF) start, baseline disease activity measures [tender joint count on 28 joints, swollen joint counts on 28 joints, HAQ score[12], erythrocyte sedimentation rate (ESR), C-reactive protein results, patient and evaluator global scores, and the relevant composite disease activity measure]. Smoking status was characterized as current smoker or ex-/never smoker. Obesity was defined as a body mass index of ≥ 30 kg/m^2 at treatment start. Serologic status was considered positive if either rheumatoid factor (RF) or anticyclic citrullinated peptide (anti-CCP) antibody were ever recorded as positive in the database. We also included sociodemographic factors, including self-reported ethnicity (white, Aboriginal, Hispanic, East Indian, Asian, African American), marital status (single, separated/widowed/divorced, or married/common-law) at anti-TNF start, and highest education level (elementary as reference, high school, college/university). We also decided to explore whether speed of attaining remission affected the ability to achieve sustained versus point remission. Subjects were classified as achieving early remission if that target was met by their first visit (< 16 weeks) after starting anti-TNF therapy.

Statistical analysis. Multivariate models for point remission and sustained remission were individually calculated for each definition to compare which variables significantly predicted attaining the outcome. All covariates were included in the initial model, with sequential removal of variables until a maximal value for the goodness-of-fit test and the percent correctly classified. All models are reported using OR. We used as-observed data only and did not impute any results. Reference categories for the sociodemographic factors were white, single marital status, and elementary education. Stata IC version 12.0 (StataCorp) was used for analyses.

RESULTS

Our population consists of 1116 biologic-naive patients treated with anti-TNF therapies who made at least 2 study visits during the study period. Details on patient demographics and baseline disease activity measures are provided in Table 1. The mean duration of followup in the

Table 1. Patient characteristics. All values mean (SD) unless specified.

Characteristics	n = 1116
Demographics	
Females; n (%)	826 (74.0)
Age at anti-TNF initiation; yrs	54.4 (13.6)
Disease duration; yrs	12.2 (10.6)
DMARD prior to anti-TNF therapy; n (SD)	2.3 (1.9)
Highest level of education (n, %)	
Elementary school	103/855 (12.0)
High school	373/855 (43.6)
University or college	379/855 (44.3)
Not reported	261/1116 (23.4)
Marital status (n, %)	
Never married or other	88/729 (12.1)
Separated, divorced, or widowed	148/729 (20.3)
Married or common-law relationship	493/729 (67.6)
Not reported	387/1116 (34.7)
Ethnicity (n, %)	
White	752/874 (86.0)
Aboriginal	60/874 (6.9)
Minority group	62/874 (7.1)
Serology	
RF-positive	637/821 (77.6)
Anti-CCP-positive	93/125 (74.4)
Baseline disease activity measures	
DAS28	6.03 (1.30)
HAQ	1.62 (0.68)
Physician global, 0–10 VAS	6.3 (1.7)
Patient global, 0–10 VAS	6.85 (2.06)
ESR, mm/h	32.9 (24.1)
CRP, mg/dl	2.18 (3.04)
CDAI	38.52 (13.59)
SDAI	40.90 (14.66)
Tender joint count (28)	14.1 (8.4)
Swollen joint count (28)	9.24 (6.1)
Therapy	
Initial agent (n, %)	
Certolizumab pegol	9 (0.7)
Etanercept	682 (54.8)
Adalimumab	212 (17.0)
Infliximab	276 (22.2)
Golimumab	25 (2.0)

Anti-TNF: anti-tumor necrosis factor-α; DMARD: disease-modifying antirheumatic drugs; anti-CCP: anticyclic citrullinated peptide antibodies; DAS28: Disease Activity Score (28 joints); HAQ: Health Assessment Questionnaire; VAS: visual analog scale; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; RF: rheumatoid factor.

cohort was 990 days (SD 745), with a median of 840 days, and a range of 44–3786 days. On average, each individual person had 6.3 visits (median 6, range 2–19).

Table 2 presents point remission rates, and sustained remission rates in patients who had attained point remission. Point remission rates varied to be as low as 26.2% for SDAI, and as high as 61.6% for DAS28. This variability was less pronounced when examining sustained remission, with the lowest rates for SDAI (19.9%) and highest for DAS28 (37.0%).

Tables detailing all covariates and OR for each remission of definition for both point and sustained durations appear in the appendices. Predictors of remission varied between disease activity measure definitions, and when comparing point and sustained remissions (Table 3). Ex-smokers and never smokers had higher odds of point remission by all definitions (OR range 1.20–2.71). Minority ethnicity decreased odds of remission by DAS28 (OR 0.13, 95% CI 0.02–0.86, p = 0.034) and CDAI (OR 0.09, 95% CI 0.01–0.80, p = 0.030). Male sex was associated with DAS28 remission (OR 2.85, 95% CI 1.59–5.10, p < 0.001), whereas higher baseline physician global [OR 0.67 per unit on a 0–10 visual analog scale (VAS), 95% CI 0.51–0.88, p = 0.004] and ESR values (OR 0.98 per mm/h, 95% CI 0.96–1.00, p =

Table 2. Remission rates, by disease activity definition. Data are n (%).

Definition	Point Remission (whole cohort)	Sustained Remission in Patients Achieving Point Remission	Sustained Remission (whole cohort)
DAS28	676/1097 (61.6)	236/638 (37.0)	236/1097 (21.5)
ACR no labs	423/1104 (38.3)	119/403 (29.5)	119/1104 (10.8)
ACR/EULAR Boolean	349/1060 (32.9)	72/294 (24.5)	72/1060 (6.8)
CDAI (≤ 2.8)	413/1009 (40.9)	100/360 (27.8)	100/1009 (9.9)
SDAI (≤ 3.3)	204/779 (26.2)	35/176 (19.9)	35/779 (4.5)

DAS28: Disease Activity Score (28 joints); ACR: American College of Rheumatology; EULAR: European League Against Rheumatism; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index.

Table 3. Independent predictors of remission, by definition and duration of remission. Exact estimates and all model variables are in the supplemental data.

Duration of Remission		Independent Predictors	Direction of Effect on Odds
Point remission			
	DAS28	Male sex	↑
		Ex-/never smoker	↑
		Minority ethnicity	↓
		Higher baseline physician global	↓
		Higher baseline ESR	↓
	ACR/EULAR Boolean	Ex-/never smoker	↑
	ACR/EULAR Boolean excluding acute-phase reactant	Ex-/never smoker	↑
		Minority ethnicity	↓
	CDAI	Ex-/never smoker	↑
		Minority ethnicity	↓
		Higher baseline patient global	↓
		Higher swollen joint count	↓
	SDAI	Higher baseline HAQ	↓
		Ex-/never smoker	↑
		University/college education	↑
Sustained remission			
	DAS28	Higher baseline physician global	↓
	ACR/EULAR Boolean	No predictors	
	ACR/EULAR Boolean excluding acute-phase reactant	Obesity	↓
	CDAI	Higher tender joint count	↓
	SDAI	No predictors	

DAS28: Disease Activity Score (28 joints); ACR: American College of Rheumatology; EULAR: European League Against Rheumatism; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire.

0.030) decreased odds of DAS28 remission. Higher baseline patient global score (OR 0.77 per unit on a 0–10 VAS, 95% CI 0.60–0.99, p = 0.038) and swollen joint counts (OR 0.93 per swollen joint, 95% CI 0.87–1.00, p = 0.05) were negative predictors for CDAI remission. Higher baseline HAQ (OR 0.62 per unit, 95% CI 0.38–1.00, p = 0.005) reduced odds for remission by the SDAI definition, and educational attainment increased these odds (OR 2.13 for university or college training, 95% CI 0.98–4.65, p = 0.05). Sustained remission was negatively predicted by the baseline physician global for the DAS28 (OR 0.80 per unit on a 0–10 VAS, 95% CI 0.66–0.99, p = 0.036), and higher tender joint count (OR 0.96 per tender joint, 95% CI 0.92–1.00, p = 0.05) for the CDAI. In the analysis of predictors of point remission in the ACR/EULAR Boolean definition excluding the acute-phase reactants, never smoking or quitting smoking increased odds of remission (OR 1.83, 95% CI 1.04–3.22, p = 0.037) and East Indian ethnicity was associated with decreased odds of remission (OR 0.11, 95% CI 0.01–0.89, p = 0.038). In the sustained remission model, being obese was associated with decreased odds of remission (OR 0.30, 95% CI 0.10–0.90, p = 0.032). RF status did not influence remission by any definition in the multivariate models.

We also explored whether early response to treatment, defined as achieving remission in the first 16 weeks after

anti-TNF agent initiation, could predict achieving sustained remission. In the multivariate model for the DAS28 definition, early remission was an independent predictor for sustained remission (OR 1.88, 95% CI 1.27–2.78, p = 0.002). No other variables independently predicted sustained remission.

DISCUSSION

Using a population-based biologics registry in Canada, we have determined that predictors of remission vary by both the disease activity measure used to define remission, and by whether the remission is determined cross-sectionally or longitudinally. Consistent across the definitions of point remission was the finding of ex-/never smokers having improved odds of remission, and East Indian patients having lower odds of remission. Aboriginal, Hispanic, and Asian patients also demonstrated a trend to lower odds of remission, but not reaching statistical significance. Additional predictors increasing the odds of point remission were male sex (by DAS28 remission) and university/college education (by SDAI remission). Disease activity did affect the odds of attaining point remission, although with variations by the measure used. High baseline physician global and higher ESR decreased the odds of DAS28 remission, whereas high baseline patient global and higher swollen joint counts decreased the odds of CDAI remission. High baseline HAQ scores decreased the odds of SDAI remission.

Fewer predictors could be identified in the sustained remission analysis. Only a higher baseline physician global was determined to reduce the odds of remission by the DAS28 definition, and similarly for a higher tender joint count by the CDAI definition. Using an alternative ACR/EULAR Boolean definition excluding the laboratory results, we also determined obesity to reduce odds of attaining remission. This finding supports an emerging literature on the consequences of obesity in treatment response[13].

The systematic review by Katchamart, *et al*[6] identified 18 applicable studies on predictors for cross-sectional remission. Independent variables for RA remission were male sex, young age, late-onset RA, short disease duration, nonsmoker, low baseline disease activity, mild functional impairment, low baseline radiographic damage, absence of RF and anti-CCP, low serum level of acute-phase reactant, interleukin 2 and receptor activator of nuclear factor-κB ligand at baseline, particular alleles for MTX receptors, early nonbiologic DMARD combinations, anti-TNF use, and moderate or good response to treatments in the first 6 months of disease. The included studies did not require that remission be sustained. Our analysis did not necessarily confirm all of these expected predictors, possibly related to distribution of frequency of particular patient characteristics. For example, the majority of the cohort had long-standing disease, reducing the power to detect differences in odds for patients with short disease duration; similarly the high seropositivity rate for RF means we had little power to examine the effect of being seronegative.

There are few data published on predictors of sustained remission in RA from observational cohorts. Patients able to achieve sustained remission offer critical information in the pursuit of personalized medicine and therapeutic selection. There is no accepted definition for sustained remission at this time either, other than the common definition of having achieved that state at multiple consecutive visits over a 1-year period[14,15,16]. Jayakumar, *et al* studied predictors for sustained remission in early (< 2 yrs) RA[16]. Point remission was defined as a DAS < 1.6; and sustained remission if DAS < 1.6 was met at all 3-, 4-, and 5-year followup visits. Only 11% of this cohort attained sustained remission, independently predicted by male sex, short duration of symptoms at treatment start, and having fewer tender joints at baseline. On the importance of sustained remission, less radiographic progression occurred and HAQ scores were significantly lower (0.13 vs 1.1) at the end of 5 years of followup if sustained remission was achieved. Reports of predictors of remission considering shorter periods of observation are available. In a Belgian cohort, remission at 4 months along with male sex, age, and disease duration at treatment start predicted remission at 1 year[17]. In the Danish DANBIO cohort, concomitant corticosteroid treatment, older age, low functional status at baseline, and the number of previous DMARD were negative predictors for both DAS28 and CDAI remission at 1 year[18].

This paper highlights important gaps in the current reporting of outcome measures. There is clearly a need to achieve consensus on a definition of sustained remission. This would allow clinicians and administrators to better estimate anticipated treatment outcomes and plan resource allocation. From a research perspective, there are likely better ways of defining disease activity states considering the duration of existence in various states. Perhaps models to define an "area under the curve" approach to evaluate longitudinal disease activity adapted for clinical practice would be the optimal solution for the many cohorts and disease registries in existence. Other methods, such as the multistate modeling approach as described by Tom and Farewell[19] or latent growth models as used by Norton, *et al*[20] are options for this type of evaluation. Although it is beyond the scope of our current paper to compare results obtained with these different methods and we used standard analysis methods to maintain familiarity of interpretation for the reader, we are encouraged to pursue this line of investigation.

Finally, our study provides further proof of the influence of determinants of health on RA outcomes. We have identified that people of an ethnic minority are less likely to achieve the desirable treatment outcome of remission. Patients with higher education levels do better than those with primary school and high school completion. Innova-

tions in the delivery of healthcare to reach out to populations found to have disparate outcomes are needed to create an environment where equitable health outcomes are realized.

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APPENDIX 1. OR for attaining point remission.

Variable	DAS28 Remission, OR (95% CI), p	ACR Excluding Laboratory, OR (95% CI), p	ACR Remission, OR (95% CI), p	CDAI Remission, OR (95% CI), p	SDAI Remission, OR (95% CI), p
Males	2.85 (1.59–5.10), <0.001	0.77 (0.48–1.25), 0.294	0.78 (0.46–1.33), 0.364	1.07 (0.67–1.72), 0.765	1.10 (0.65–1.87), 0.721
RF +	1.46 (0.82–2.61), 0.198	1.36 (0.83–2.21), 0.214	1.33 (0.77–2.32), 0.307	1.23 (0.75–2.02), 0.406	1.32 (0.77–2.25), 0.314
Baseline HAQ	0.70 (0.41–1.17), 0.170	0.75 (0.49–1.14), 0.172	0.75 (0.47–1.20), 0.229	0.93 (0.61–1.42), 0.736	0.62 (0.38–1.00), 0.051
Disease duration (continuous)	0.99 (0.97–1.01), 0.304	0.99 (0.97–1.01), 0.443	0.99 (0.96–1.01), 0.276	0.98 (0.96–1.00), 0.102	1.00 (0.97–1.02), 0.828
BMI ≥ 30	0.70 (0.40–1.20), 0.191	not in model	0.80 (0.46–1.37), 0.411	0.63 (0.38–1.04), 0.068	not in model
Ex-/never smoker	2.11 (1.15–3.86), 0.016	1.83 (1.04–3.22), 0.037	1.20 (1.05–3.81), 0.036	2.21 (1.25–3.90), 0.006	2.71 (1.33–5.51), 0.006
Black	not in model	not in model	not in model	not in model	not in model
Aboriginal	0.52 (0.25–1.06), 0.070	1.02 (0.52–1.99), 0.958	not in model	0.93 (0.47–1.84), 0.846	0.98 (0.46–2.08), 0.950
Hispanic	0.54 (0.09–3.16), 0.497	0.28 (0.03–2.49), 0.254	not in model	0.46 (0.08–2.65), 0.382	0.82 (0.14–4.75), 0.826
East Indian	0.13 (0.02–0.86), 0.034	0.11 (0.01–0.89), 0.038	not in model	0.09 (0.01–0.80), 0.030	0.18 (0.02–1.47), 0.108
Asian	1.29 (0.31–5.35), 0.721	0.67 (0.16–2.72), 0.573	not in model	0.52 (0.13–2.10), 0.357	0.80 (0.19–3.28), 0.754
Separated/divorced/ widowed	0.48 (0.19–1.20), 0.115	0.76 (0.34–1.69), 0.501	0.71 (0.28–1.76), 0.456	not in model	not in model
Married/common law	0.71 (0.32–1.61), 0.417	1.23 (0.62–2.43), 0.557	1.25 (0.57–2.72), 0.577	not in model	not in model
High school	1.27 (0.63–2.53), 0.504	1.06 (0.56–2.03), 0.854	1.32 (0.60–2.89), 0.485	not in model	1.37 (0.64–2.98), 0.419
University/college	1.49 (0.73–3.05), 0.276	1.67 (0.86–3.23), 0.127	2.02 (0.92–4.45), 0.081	not in model	2.13 (0.98–4.65), 0.057
Baseline Applicable Composite Disease Activity Measure	1.01 (0.57–1.82), 0.965	not applicable	not applicable	1.05 (0.99–1.12), 0.131	0.56 (0.52, 1.44), 0.990
Baseline physician global	0.67 (0.51–0.88), 0.004	not in model	not in model	0.86 (0.69–1.06), 0.145	1.75 (1.62, 2.30), 0.991
Baseline patient global	1.21 (1.03–1.42), 0.020	1.01 (0.89–1.14), 0.912	1.04 (0.91–1.19), 0.557	0.77 (0.60–0.99), 0.038	1.84 (1.70, 2.21), 0.990
Baseline ESR	0.98 (0.96–1.00), 0.030	not in model	not in model	not in model	1.00 (0.99–1.01), 0.805
Baseline CRP	1.00 (0.90–1.11), 0.994	not in model	0.98 (0.89–1.07), 0.655	not in model	1.77 (1.64, 2.27), 0.90
Total tender joints	1.00 (0.95–1.06), 0.933	1.02 (0.99–1.05), 0.314	1.00 (0.96–1.03), 0.775	0.98 (0.92–1.04), 0.546	1.81 (1.67, 2.25), 0.990
Total swollen joints	1.02 (0.95–1.08), 0.605	0.98 (0.94–1.03), 0.430	0.98 (0.93–1.03), 0.328	0.93 (0.87–1.00), 0.057	1.70 (1.58, 2.34), 0.991
Constant	7.35 (0.82–66.10), 0.075	0.33 (0.09–1.21), 0.095	0.23 (0.05–1.01), 0.051	1.54 (0.43–5.47), 0.509	0.22 (0.04–1.10), 0.065
Goodness of fit (best close to 1)	0.5883	0.3306	0.4934	0.6977	0.8848
Classification test	70.20%	68.13%	72.66%	64.42%	71.05%

DAS28: Disease Activity Score (28 joints); HAQ: Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; RF: rheumatoid factor; ACR: American College of Rheumatology; BMI: body mass index.

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APPENDIX 2. OR for attaining sustained remission.

Variable	DAS28 Remission, OR (95% CI), p	ACR Excluding Laboratory, OR (95% CI), p	ACR Remission, OR (95% CI), p	CDAI Remission, OR (95% CI), p	SDAI Remission no final, initial used, OR (95% CI), p
Males	0.84 (0.46–1.50), 0.549	1.32 (0.56–3.12), 0.529	not in model	not in model	0.45 (0.14–1.46), 0.185
RF +	0.93 (0.49–1.74), 0.814	1.25 (0.47–3.33), 0.659	not in model	0.51 (0.23–1.15), 0.105	0.68 (0.20–2.32), 0.538
Baseline HAQ	1.24 (0.76–2.03), 0.391	0.74 (0.33–1.65), 0.456	not in model	not in model	0.83 (0.29–2.57), 0.748
Disease duration (continuous)	0.98 (0.96–1.01), 0.276	0.98 (0.94–1.03), 0.425	not in model	not in model	1.00 (0.94–1.06), 0.894
BMI ≥ 30	not in model	0.30 (0.10–0.90), 0.032	not in model	not in model	0.42 (0.10–1.68), 0.218
Ex-/never smoker	not in model	3.28 (0.78–13.86), 0.107	not in model	2.11 (0.66–6.79), 0.211	1.67 (0.26–10.78), 0.588
Black	not in model	not in model	not in model	not in model	not in model
Aboriginal	not in model	not in model	not in model	not in model	1.08 (0.18–6.45), 0.937
Hispanic	not in model	not in model	not in model	not in model	not in model
East Indian	not in model	not in model	not in model	not in model	not in model
Asian	not in model	not in model	not in model	not in model	not in model
Separated/divorced/ widowed	2.61 (0.85–7.95), 0.093	not in model	8.94 (0.79–101.5), 0.077	1.78 (0.72–4.38), 0.212	0.58 (0.07–4.70), 0.609
Married/common law	2.52 (0.94–6.71), 0.065	not in model	4.29 (0.49–37.10), 0.186	not in model	0.63 (0.11–3.66), 0.607
High school	not in model	not in model	not in model	not in model	0.71 (0.11–4.77), 0.724
University/college	not in model	not in model	2.09 (0.80–5.44), 0.133	not in model	0.74 (0.11–5.19), 0.764
Baseline disease activity score	not in model	not in model	not in model	not in model	not in model
Baseline physician global	0.80 (0.66–0.99), 0.036	0.96 (0.67–1.38), 0.835	not in model	not in model	1.34 (0.78–2.30), 0.289
Baseline patient global	not in model	1.07 (0.84–1.37), 0.582	not in model	not in model	1.00 (0.71–1.39), 0.985
Baseline ESR	not in model	1.00 (0.98–1.02), 0.984	not in model	not in model	1.01 (0.99–1.04), 0.345
Baseline CRP	not in model	1.06 (0.88–1.26), 0.550	1.15 (0.98–1.36), 0.083	not in model	0.83 (0.61–1.12), 0.217
Total tender joints	not in model	0.98 (0.91–1.04), 0.448	not in model	0.96 (0.92–1.00), 0.051	0.94 (0.86–1.03), 0.165
Total swollen joints	not in model	0.93 (0.84–1.03), 0.170	not in model	not in model	0.94 (0.81–1.10), 0.450
Constant	1.29 (0.28–5.93), 0.743	0.55 (0.05–5.64), 0.615	0.04 (0.00–0.40), 0.006	0.59 (0.15–2.36), 0.453	0.54 (0.01–36.30), 0.773
Goodness of fit (best close to 1)	0.3764	0.2322	0.3434	0.6194	0.9957
Classification test	65.22%	73.20%	77.06%	70.81%	78.76%

DAS28: Disease Activity Score (28 joints); HAQ: Health Assessment Questionnaire; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; CDAI: Clinical Disease Activity Index; SDAI: Simplified Disease Activity Index; RF: rheumatoid factor; ACR: American College of Rheumatology; BMI: body mass index.

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