

**Supplementary Table S1. Baseline characteristics in the 222 patients**

	Median [25th-75th] or category: Number (%)*	Missing counts (%)
Age, years	53.9 [42.0-62.6]	0 (0)
Sex*	Female: 137 (62%), Male: 85 (38%)	0 (0)
BMI, kg/m <sup>2</sup>	25.5 [22.9-28.2]	2 (0.9)
Smoking*	Never: 75 (34%), Ever: 93 (42%), Present: 54 (24%)	0 (0)
Disease duration, months	5.45 [2.8-9.9]	0 (0)
ACPA*	Positive: 182 (82%), Negative: 40 (18%)	0 (0)
RF*	Positive: 157 (71%), Negative: 65 (29%)	0 (0)
DAS	3.3 [2.6-4.2]	0 (0)
RAI	7.0 [4.0-12.8]	0 (0)
SJC44	9.5 [4.0-14.8]	0 (0)
PGA, VAS 0-100mm	49.0 [31.0-69.8]	0 (0)
PhGA, VAS 0-100mm	36.0 [23.0-55.0]	1 (0.5)
ESR, mm/h	19.0 [11.0-30.8]	1 (0.5)
CRP, mg/L	7.0 [3.0-18.0]	0 (0)
Joint pain, VAS 0-100mm	46.5 [29.0-70.0]	0 (0)
Fatigue, VAS 0-100mm	38.0 [14.2-64.8]	0 (0)
PROMIS-PF	39.6 [32.9- 44.2]	0 (0)
CDAI	21.2 [14.8-30.9]	1 (0.5)
SDAI	22.2 [15.7-33.2]	1 (0.5)
RAID score	4.4 [2.9-6.0]	2 (0.9)
Methotrexate starting dose, mg/week	15.0 [15.0-15.0]	0 (0)

Values are median [25<sup>th</sup>-75<sup>th</sup> percentile] unless indicated as number (%) by an asterisk (\*) for categorical characteristics including Sex (male/female), Smoking (never/ever/present), ACPA (positive/negative) and RF (positive/negative). DAS = Disease Activity Score based on ESR, patient global, SJC 44 and Ritchie Articular Index. ACR = American College of Rheumatology, EULAR = The European Alliance of Associations for Rheumatology, Disease duration = Time since patient reported first swollen joint measured as months, PROMIS-PF = Patient-Reported Outcome Measurement Information Score short form v1.0-physical function 20a T-score with a mean of 50 and standard deviation of 10 in a reference population. ACPA = anti-cyclic citrullinated peptide, RF = Rheumatoid Factor, BMI = Body Mass Index, SDAI = Simplified Disease Activity Index, CDAI = Clinical Disease Activity Index, SJC44 = Swollen Joint Count in 44 joints, VAS = Visual Analogue Scale, PGA = Patients Global Assessment of disease activity, PhGA = Physician Global Assessment of disease activity, RAI = Tender joint count (Ritchie Articular Index, score 0-78), ESR = Erythrocyte Sedimentation Rate, CRP = C Reactive Protein, RAID = Rheumatoid Arthritis Impact of Disease.

**Supplementary Table S2. Definition and statistics of predicted clinical outcomes used in the analyses**

<b>Treatment outcomes</b>	<b>Count, Proportion</b>	<b>Definition</b>
ACR/EULAR Boolean non-remission at 6 months	143, 64%	The patient must comply with all: <ul style="list-style-type: none"> <li>• RAI <math>\leq 1</math></li> <li>• SJC28 <math>\leq 1</math></li> <li>• CRP <math>\leq 1</math> mg/dl</li> <li>• PGA <math>\leq 1</math></li> </ul> in order to achieve ACR/EULAR remission otherwise non-remission
SDAI non-remission at 6 months	134, 60%	SDAI = TJC28 + SJC28 + PGA/10 + PhGA/10 + CRP/10 Remission: $\leq 3.3$ Otherwise non-remission
CDAI non-remission at 6 months	135, 61%	CDAI = TJC28 + SJC28 + PGA/10 + PhGA/10 Remission: $\leq 2.8$ Otherwise non-remission

ACR = American College of Rheumatology, EULAR = The European Alliance of Associations for Rheumatology, SDAI = Simplified Disease Activity Index, CDAI = Clinical Disease Activity Index, RAI= Tender joint count (Ritchie Articular Index, score 0-78), SJC28 = Swollen Joint Count in 28 joints, SJC44 = Swollen Joint Count in 44 joints , CRP = C Reactive Protein, PGA = Patients Global Assessment of disease activity, PhGA = Physician Global Assessment of disease activity, TJC28 = Tender Joint Count in 28 joints.

**Supplementary Table S3: Statistics of characteristics of patients grouped as remission and non-remission based on specified criteria.**

Characteristics	ACR/EULAR Boolean non-remission at 6 months		SDAI non-remission at 6 months		CDAI non-remission at 6 months	
	Remission (36%)	Non-remission (64%)	Remission (40%)	Non-remission (60%)	Remission (39%)	Non-remission (61%)
Age, years	51.4 [38.5-63.0]	54.7 [43.5-62.5]	52.4 [39.8-61.8]	54.9 [44.0-62.7]	51.9 [39.6-62.6]	55.0 [44.2-62.5]
Sex*						
-Female	52 (65.8%)	85 (59.4%)	55 (62.5%)	82 (61.2%)	55 (63.2%)	82 (60.7%)
-Male	27 (34.2%)	58 (40.6%)	33 (37.5%)	52 (38.8%)	32 (36.8%)	53 (39.3%)
BMI, kg/m2	24.9 [21.9-27.9]	25.7 [23.5-28.4]	25.0 [22.0-27.5]	25.7 [23.4-28.6]	25.2 [22.0-27.5]	25.5 [23.0-28.6]
Smoking*						
-Never	26 (32.9%)	49 (34.3%)	30 (34.1%)	45 (33.6%)	32 (36.8%)	43 (31.9%)
-Ever	32 (40.5%)	61 (42.7%)	34 (38.6%)	59 (44.0%)	31 (35.6%)	62 (45.9%)
- Present	21 (26.6%)	33 (23.1%)	24 (27.3%)	30 (22.4%)	24 (27.6%)	30 (22.2%)
Disease duration, months	5.4 [3.2-10.7]	5.5 [2.7-9.8]	6.1 [3.2-10.9]	5.0 [2.7-9.7]	6.1 [3.1-10.7]	5.4 [2.7-9.8]
ACPA*						
-Positive	64 (81.0%)	118 (82.5%)	71 (80.7%)	111 (82.8%)	70 (80.5%)	112 (83.0%)
-Negative	15 (19.0%)	25 (17.5%)	17 (19.3%)	23 (17.2%)	17 (19.5%)	23 (17.0%)
RF*						
-Positive	52 (65.8%)	105 (73.4%)	59 (67.0%)	98 (73.1%)	58 (66.7%)	99 (73.3%)
-Negative	27 (34.2%)	38 (26.6%)	29 (33.0%)	36 (26.9%)	29 (33.3%)	36 (26.7%)
DAS	2.9 [2.3-3.5]	3.6 [2.9-4.5]	2.9 [2.3-3.5]	3.7 [2.9-4.5]	3.0 [2.3-3.5]	3.6 [2.8-4.5]
RAI	4.0 [2.5-8.0]	8.0 [5.0-15.0]	4.5 [3.0-8.0]	9.0 [5.0-14.8]	5.0 [3.0-9.0]	8.0 [4.5-14.0]
SJC44	8.0 [4.0-13.0]	10.0 [5.0-15.0]	9.0 [4.0-13.0]	10.0 [5.0-15.8]	10.0 [4.0-13.5]	9.0 [5.0-15.0]
PGA, VAS 0-100mm	34.0 [21.0-52.5]	54.0 [37.5-75.0]	34.5 [21.8-53.0]	55.0 [38.0-76.0]	35.0 [21.0-53.0]	54.0 [37.5-76.5]
PhGA, VAS 0-100mm	30.0 [19.5-42.0]	41.5 [28.0-61.8]	31.0 [20.0-42.5]	42.5 [27.2-63.5]	31.5 [20.0-45.0]	41.0 [26.5-60.5]
ESR, mm/h	16.5 [11.0-27.0]	21.0 [12.0-33.5]	16.0 [10.0-27.0]	21.5 [12.2-35.8]	17.0 [10.0-27.8]	21.0 [12.0-33.5]
CRP, mg/L	5.0 [2.4-10.0]	8.9 [4.0-19.0]	5.0 [2.9-10.5]	9.0 [4.0-21.8]	6.0 [3.0-14.0]	8.0 [4.0-19.0]
Joint pain, VAS 0-100mm	33.0 [21.0-50.5]	53.0 [33.0-73.0]	34.0 [22.8-51.2]	55.0 [33.2-74.0]	34.0 [21.0-51.5]	55.0 [33.5-74.0]
Fatigue, VAS 0-100mm	27.0 [6.5-46.5]	48.0 [24.5-69.0]	27.5 [4.0-46.2]	49.0 [25.0-69.8]	26.0 [3.5-46.0]	50.0 [25.0-70.5]
PROMIS-PF	43.1 [37.3-47.8]	36.1 [30.5-41.6]	42.6 [37.6-46.6]	35.3 [30.1-42.1]	42.6 [37.3-46.6]	35.7 [30.3-42.1]
CDAI	17.3 [9.6-24.2]	24.2 [17.2-34.2]	17.4 [10.3-25.2]	24.4 [17.2-34.3]	17.5 [10.2-26.1]	24.2 [16.6-34.1]
SDAI	18.1 [10.0-25.0]	25.9 [17.8-36.5]	18.4 [11.4-25.9]	26.1 [17.7-36.7]	18.8 [11.4-26.6]	24.9 [17.4-36.4]
RAID score	2.9 [2.0-4.4]	5.3 [3.9-6.6]	3.0 [2.0-4.5]	5.3 [4.0-6.7]	3.0 [2.0-4.4]	5.3 [4.0-6.8]

Methotrexate starting dose, mg/week	15.0 [15.0-15.0]	15.0 [15.0-15.0]	15.0 [15.0- 15.0]	15.0 [15.0-15.0]	15.0 [15.0- 15.0]	15.0 [15.0- 15.0]
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Baseline clinical characteristics of the included patients are presented for both groups. Continuous variables are reported as the median [25th–75th percentile], whereas categorical variables, marked with an asterisk (\*), are presented as n (percentage).

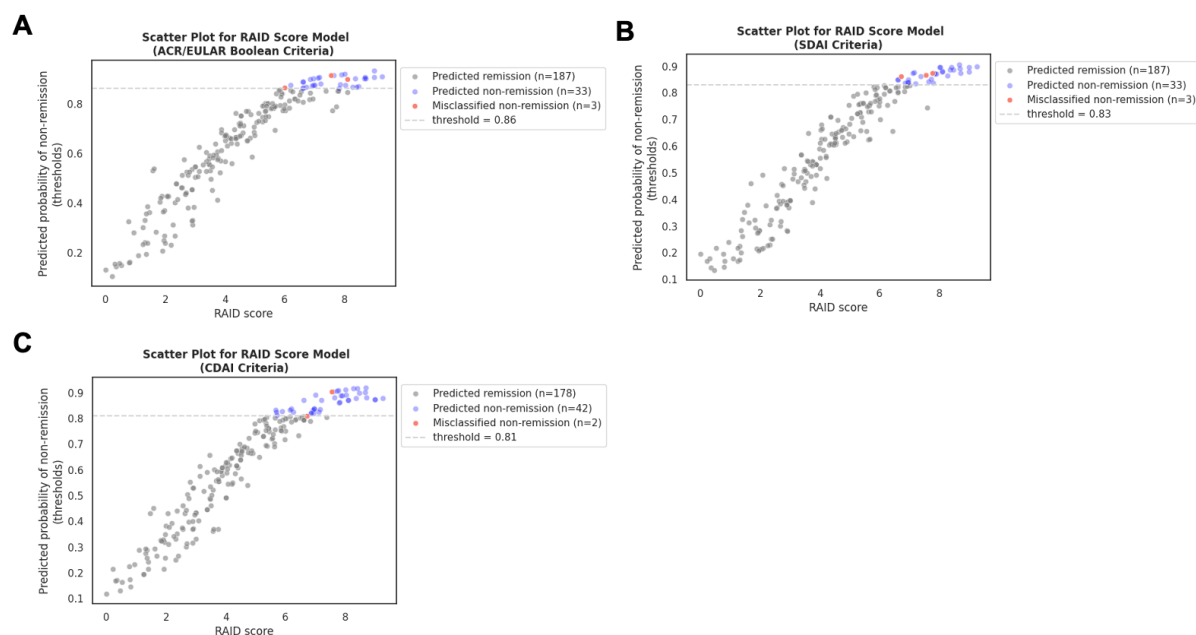
**Supplementary Table S4: Hyperparameters for grid search strategy to optimize prediction models.**

Base algorithms	Hyperparameters for Grid Search
Elastic Net	<ul style="list-style-type: none"> <li>'C': [0.001, 0.01, 0.1, 0.5, 1, 5, 10, 100]</li> <li>'l1_ratio': [0.001, 0.01, 0.1, 0.3, 0.5, 0.7, 0.9, 0.999],</li> <li>Other hyperparameters: 'penalty': 'elastic net', 'solver': 'saga', 'max_iter': 5000.</li> </ul>
Random Forest	<ul style="list-style-type: none"> <li>'max_depth': [5, 7, 10],</li> <li>'n_estimators': [75, 100, 125, 150]</li> <li>'min_samples_split': [3, 4]</li> <li>'max_features': ['sqrt']</li> </ul>
Support vector machine	<ul style="list-style-type: none"> <li>'gamma': ['scale', 'auto']</li> <li>'kernel': ['linear', 'poly', 'sigmoid']</li> <li>'C': [0.001, 0.01, 0.1, 0.5, 1, 10]</li> </ul>

**Supplementary Table S5. Performance evaluation across five trials.**

	ACR/EULAR non-Remission	SDAI non-Remission	CDAI non-Remission
<b>Trial 1</b>	0.75(0.08)	0.77(0.02)	0.76(0.06)
<b>Trial 2</b>	0.73(0.06)	0.75(0.12)	0.77(0.05)
<b>Trial 3</b>	0.75(0.03)	0.77(0.04)	0.75(0.07)
<b>Trial 4</b>	0.77(0.07)	0.73(0.05)	0.75(0.04)
<b>Trial 5</b>	0.72(0.11)	0.76(0.04)	0.76(0.04)

The AUC-ROC metrics for each trial presented as the mean with the standard deviation are displayed.  
AUC-ROC = The area under the receiver operating characteristic curve.



**Supplementary Figure S1: Association between RAID score and predicted probability of non-remission.** The scatter plot illustrates the relationship between RAID score and predicted probabilities of non-remission based on (A) ACR/EULAR Boolean-, (B) SDAI-, (C) CDAI-criteria using a simplified model that exclusively incorporates the RAID score. Strict thresholds of 0.86, 0.83 and 0.81, identified earlier, are shown with a dashed line respective to each criterion. Blue dots represent predicted non-remission, with misclassified non-remission marked in red.

## **Supplementary Data**

### **Supplementary Data S1. Data imputation for missing outcomes of ACR/EULAR-, SDAI, CDAI-remission status.**

Among the 222 patients included in the study, 12 patients had missing outcomes for ACR/EULAR- and CDAI-remission status. On the other hand, SDAI-remission status was missing for 13 patients, and 16 patients had missing outcomes for DAS-based EULAR non-response. To address these missing outcome variables, data imputation was performed using the following rules; for non-remission outcomes at 6 months: non-remission was determined for patients with missing follow-up visits between 6 and 24 months. Remission was determined if the DAS score was  $< 1.2$  and the patient was on methotrexate monotherapy (including standard and optimized doses) at the 4- and 12-month visits. Patients who continued to receive methotrexate monotherapy (including standard and optimized doses) from 12 to 24 months were considered to be in remission.

### **Supplementary Data S2. Hyperparameter tuning using grid search strategy and cross-validation.**

Hyperparameter tuning is a crucial part of model training process. This was conducted on the model development folds, comprising 80% of total dataset, which has been segmented through nested cross-validation. To achieve the optimal hyperparameter of each base model, grid search strategy combined with cross-validation was used to optimize each model's performance. The grid search aimed to maximize the AUC-ROC by evaluating various combinations of hyperparameters (refer to supplementary Table 4), and 5-fold cross-validation within the grid search process was employed to improve the model generalization. Subsequently, models configured with optimal hyperparameters were initialized for super learner modeling.