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REVIEW

# Artificial intelligence to predict treatment response in rheumatoid arthritis and spondyloarthritis: a scoping review

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## Abstract

To analyse the types and applications of artificial intelligence (AI) technologies to predict treatment response in rheumatoid arthritis (RA) and spondyloarthritis (SpA). A comprehensive search in Medline, Embase, and Cochrane databases (up to August 2024) identified studies using AI to predict treatment response in RA and SpA. Data on study design, AI methodologies, data sources, and outcomes were extracted and synthesized. Findings were summarized descriptively. Of the 4257 articles identified, 89 studies met the inclusion criteria (74 on RA, 7 on SpA, 4 on Psoriatic Arthritis and 4 a mix of them). AI models primarily employed supervised machine learning techniques (e.g., random forests, support vector machines), unsupervised clustering, and deep learning. Data sources included electronic medical records, clinical biomarkers, genetic and proteomic data, and imaging. Predictive performance varied by methodology, with accuracy ranging from 60 to 70% and AUC values between 0.63 and 0.92. Multi-omics approaches and imaging-based models showed promising results in predicting responses to biologic DMARDs and JAK inhibitors but methodological heterogeneity limited generalizability. AI technologies exhibit substantial potential in predicting treatment responses in RA and SpA, enhancing personalized medicine. However, challenges such as methodological variability, data integration, and external validation remain. Future research should focus on refining AI models, ensuring their robustness across diverse patient populations, and facilitating their integration into clinical practice to optimize therapeutic decision-making in rheumatology.

**Keywords** Artificial intelligence · Machine learning · Rheumatoid arthritis · Spondyloarthritis · Treatment response · Scoping review

## Introduction

Rheumatoid arthritis (RA) and spondyloarthritis (SpA) are chronic inflammatory diseases that significantly impact patients' quality of life and pose a significant burden on healthcare systems [1–3]. Both conditions have heterogeneous treatment responses, despite advances in treatment, predicting individual responses remains a challenge, and costing global healthcare systems $162 billion annually due to prolonged therapeutic trial-and-error approaches that delays optimal disease management. While biologic and targeted synthetic DMARDs have transformed care, 30–40% of patients exhibit inadequate responses to first line therapies, delaying disease control by 6–12 months on average [4]. This unpredictability stems from complex interactions between genetic, proteomic, and environmental factors that conventional statistical methods often fail to unravel. Artificial intelligence (AI) has emerged as a transformative force in rheumatology, offering an opportunity to refine treatment strategies by leveraging large-scale data analysis to identify predictive response factors. Machine learning (ML) and deep learning (DL), have demonstrated the potential to uncover complex patterns in clinical, genetic,

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and imaging data, providing novel insights that traditional statistical methods might overlook [5, 6]. AI-driven models have been increasingly explored for their ability to enhance personalized medicine, optimize therapeutic decisions, and improve patient outcomes. However, AI's methodologies, data sources, and applications in predicting treatment response vary widely across studies, creating the need for a structured synthesis of existing evidence.

This scoping review (ScR) aims to provide a comprehensive overview of the current landscape of AI applications in predicting treatment responses in RA and SpA. We examined the methodologies employed, the data types analysed, and the key findings from recent studies.

## Methods

A ScR methodology was selected. Instead of predefined research questions, our team aimed to map key concepts, primary sources, and types of evidence available in the literature on the use and applications of AI/ML [7] for predicting response to treatment in RA, SpA (including PsA patients). The review adheres to the PRISMA Extension for Scoping Reviews [8] (See Supplementary Material, Table S1). The protocol of this review was registered on figshare.com [9].

### Search strategy and selection criteria

A broad search strategy was designed for digital tools to predict treatment response in RA and SpA (including PsA). Health research databases were selected, including Medline via PubMed, Embase, and Cochrane Library. Search terms were relevant to four themes: artificial intelligence, machine learning, treatment response, rheumatoid arthritis and spondyloarthritis, and the search was adapted to suit each database (see Tables S2, S3 and S4 in Supplementary Material for details). The ScR was structured using the PICOt framework to guide the search strategy and inclusion criteria: Adult patients diagnosed with RA, SpA or PsA (P); application of AI or ML techniques for predicting treatment response (I); and prediction of treatment response, including but not limited to remission rates, disease activity scores and treatment persistence (O) (Comparison was not applicable, as this ScR aimed to map the current landscape of AI applications, rather than compare specific interventions). The reference lists of all articles selected for review were manually searched for additional articles. The investigation was conducted on 30th August 2024, and no publication date or language limitations were set.

Any article reporting on the characteristics and applications of AI/ML in evaluating treatment response in RA and SpA (systematic reviews, randomized clinical trials, and observational studies) was deemed eligible. Articles were excluded if they did not report an original contribution to the research topic, had no full text available, or if the ML was applied in other phases of the study (in the classification by clusters, for example) and not in the analysis of response to treatment.

One reviewer (TO) independently searched the electronic databases and screened the articles using the search strategy. The second author (LC) blindly double-screened 100% of the articles by title and abstract and 10% of the full-text articles, obtaining a 100% agreement rate with the first reviewer.

### Data analysis and risk of bias assessment

Data were extracted using a standardised template form designed for this research. A narrative review synthesis method was selected. As ScRs aim to provide an overview of the existing evidence regardless of methodological quality or risk of bias, and no critical appraisal is compulsory [7, 8]. However, we decided to analyse the quality of the included papers using the PROBAST scale [10]. Given the absence of predefined hypotheses, a meta-analysis was not considered appropriate for this review.

## Results

The search strategies resulted in 4257 articles (1489 duplicates), 89 of which were finally included. Among the included articles, 45 were retrospective observational studies, 36 were prospective observational studies, 8 utilized clinical trial data (either through specific clinical trial designs, secondary analyses of previous trials, or combined analyses of multiple trials). In the supplementary material, we have included the excluded articles and the reasons for exclusion after full-text reading (Table S5).

Table 1 outlines the key characteristics of the included studies, including their duration and data sources. Regarding the diseases studied, 74 articles focused exclusively on patients with RA, 7 on SpA,1 on both RA and SpA, and 3 included patients with RA, SpA, and psoriatic arthritis (PsA). Additionally, 4 studies focused exclusively on patients with a diagnosis of PsA. We also included the inclusion criteria for the articles if they are mentioned. In the supplementary material (Table S6), we have incorporated the quality analysis of the included articles using the PROBAST tool.

The included studies (see details in Table 2) analysed a wide range of pharmacological treatments for RA, SpA, and PsA, with a focus on identifying predictors of treatment efficacy across conventional synthetic DMARDs (csDMARDs), biologic DMARDs (bDMARDs), and targeted synthetic DMARDs (tsDMARDs). Methotrexate (MTX) was the most extensively studied csDMARDs, with predictors

**Table 1** Evidence table of included articles

| Study | Design | Duration of follow-up | Source of data | Disease | n participants |
|---|---|---|---|---|---|
| Alsaber, 2023 [11] | P | 1 y | KRRD | RA | 1000 |
| Aripova, 2022 [12] | R | 6 m | CERTAIN study | RA | 1092 |
| Bai, 2023 [13] | R | 2 y | EMR and outpatient review records | RA | 154 |
| Bouget, 2022 [14] | R | 12 m | ESPOIR, Leiden Cohort, tREACH | RA | 821 |
| Bouget_2022_3 [15] | P | 11 y (+18 m) | RA ESPOIR cohort | RA | 279 |
| Brizzi, 2019 [16] | R | Not mentioned | U-Act-Early trial population | RA | Not mentioned |
| Burkard, 2022 [17] | R | 15 m | SCQM | RA | 3516 |
| Casaburi, 2022 [18] | P | 3 m | Synovial biopsies and outcome data | RA | 95 |
| Chen, 2019 [19] | CT | 14 w | EMR | RA | 20 |
| Cherlin, 2019 [20] | R | 6 m | MATURA | RA | Not mentioned |
| Cho, 2024 [21] | P | 12 w | EMR and lab | RA | 88 |
| Cohen_2021_3 [22] | P | 24 w | Blood samples | RA | 391 targeted therapy-naïve patients |
| Curtis, 2023 [23] | R | 12 m | RISE Rheumatology Registry | RA | 2949 |
| Dalen, 2023 [24] | R | Not mentioned (max register 7 y) | PDR, NPR, and Causes of Death Register | RA, SpA, PsA | 13,913 |
| Dervieux, 2012 [25] | R | 53.6 m | Three cohorts (USA; The Netherlands and Sweden) | RA | 971 |
| Duong_2022_2 [26] | RCT | 24 w | RCT | RA | 775 |
| Duquesne, 2022 [27] | P | 9 m | ESPOIR cohort, EAC cohort, and the tREACH trial | RA | 674 patients with 732 therapeutic sequences |
| Fadaei, 2023 [28] | R | 24 m | U-Act-Early trial population | RA | 299 |
| Fernandez, 2023 [29] | R | individual follow-up durations | BIOBADASER database | SpA | 969 |
| Garcia-Dorta, 2021 [30] | P | 5 y | Database maintained by three Hospitals in the Canary Islands | SpA | 138 |
| Gosselt, 2021 [31] | RCT | 3 m | tREACH and the U-Act-Early trial | RA | 355 |
| Gottlieb, 2021 [32] | MA-RCT | 24 w | FUTURE 2, FUTURE 3, FUTURE 4, and FUTURE 5 phase 3 clinical trials | PsA | 2049 |
| Guan, 2019 [33] | R | 24 m | DREAM | RA | 1,892 |
| Hageman, 2023 [34] | R | 3 to 6 m | Clinical database | RA | 92 |
| Icten, 2022 [35] | R | 8 m | OM1 RA Registry | RA | 6648 |
| Jin, 2019 [36] | R | 1 y | Optum Market Clarity database | RA | 24,871 |
| Johansson, 2021 [37] | R | 24 w | Corrona RA registry and four RCTs (ACT-RAY, FUNCTION, ADACTA, and AMBITION) | RA | RCTs: 853 participants, RWD: 452 participants using TCZ, 3,204 participants |
| Ju, 2021 [38] | R | 12 m | DREAM data | RA | 2706 |
| Kalweit, 2023 [39] | R | 15 m | SCQM registry | RA | 3516 |
| Kato, 2021 [40] | P | 12 w | Clinical assessments and ultrasound evaluations | RA, SpA, PsA | 100 |
| Kim, 2021 [41] | P | 6 m | EMR | RA | 98 |

**Table 1** (continued)

| Study | Design | Duration of follow-up | Source of data | Disease | n participants |
|---|---|---|---|---|---|
| Kim, 2023 [42] | P | 6 m | EMR | RA | 110 |
| Kim, 2024 [43] | P | 12 m | KOBIO | RA | aTNF (n = 574)<br>JAKi (n = 209) |
| Kimpton, 2022 [44] | R | 5 y | EMR and lab | RA | 112 |
| Koo, 2021 [45] | P | 0,97 y | KOBIO | RA | 1204 |
| Lee_2021_2 [46] | P | 1 y or more | KOBIO | RA, SpA | RA: 625 training + 322 test = 947 total;<br>AS: 611 training + 296 test = 907 total |
| Liede, 2022 [47] | R | 1 y | Optum Market Clarity data | RA | 2018 |
| Liede_2022_2 [48] | R | 2 y | Optum Market Clarity data | RA | 24,871 |
| Lim, 2022 [49] | R | 2 y | Lab kits | RA | 349 |
| Lim_2022_2 [50] | R | 2 y | Tan Tock Seng Hospital RA Registry | RA | 349 |
| Lopez-Pedrera, 2024 [51] | P | 3 m | EMR | RA | 123 RA patients + 27 healthy donors |
| Luque, 2021 [52] | P | 6 m | Clinical records | RA | 104 RA patients + 29 healthy donors |
| Maarseveen, 2022 [53] | P | Not mentioned | Clinical records | RA | 944 |
| Maciejewski, 2021 [54] | P | 6 m | RAMS | RA | 100 |
| Magrey, 2021 [55] | CT | 1 y | SELECT-AXIS 1 study | SpA | 187 |
| Matsuo, 2022 [56] | P | 2 y | KURAMA cohort | RA | 210 |
| Mellors, 2020 [57] | P | 6 m | Lab database and clinical measurements from the CERTAIN trial | RA | 376 |
| Messelink, 2021 [58] | R | Not mentioned | UPOD | RA | 1873 |
| Miyoshi, 2016 [59] | P | 14 w | Clinical records | RA | 180 |
| Morid, 2021 [60] | R | 1 y | IQVIA database | RA | 120,237 |
| Myasoedova, 2021 [61] | P | 3 m | PAMERA | RA | 643 |
| Najm, 2021 [62] | P | 12 m | Scottish Early Rheumatoid Arthritis SERA cohort | RA | 99 |
| Nishimoto, 2010 [63] | R | 24 w | SATORI study (Lab samples) | RA | 228 (197 genes) |
| Oberg Sysojev, 2024 [64] | R | 3 y | SRQ and EIRA study | RA | 3128 |
| Perton, 2024 [65] | CT | 16 w | TOFA-PREDICT trial | PsA | 80 |
| Phillips, 2023 [66] | P | Not mentioned | Rheumatology Biologics database | RA | 663 |
| Plant_2019_2 [67] | P | 6 m | RAMS | RA | 82 |
| Prasad, 2022 [68] | P | 6 m | Lab database | RA | 89 |
| Prenga, 2023 [69] | P | 1 y | DANBIO registry | RA | 685 |
| Queiro, 2022 [70] | P | 2 y | REAPSER | PsA | 158 |
| Rehberg, 2021 [71] | R | 24 w | MOBILITY, MONARCH, TARGET, and ASCERTAIN | RA | 63 participants in the MOBILITY trial were used for training and cross-validation; total number across all trials not specified in text quotes |
| Ritcher, 2016 [72] | R | 15 y | RABBIT register | RA | 1781 |
| Rivellese, 2022 [73] | RCT | 48 w | Peripheral blood | RA | 164 |
| Ruiz Romero, 2018 [74] | P | 6 m | PEAC | RA | 30 |
| Salehi, 2024 [75] | P | 12 m | Clinical records and lab | RA | 154 |
| Shipa, 2022 [76] | R | 32.6 m | Clinical records | SpA | 188 |

**Table 1** (continued)

| Study | Design | Duration of follow-up | Source of data | Disease | n participants |
|---|---|---|---|---|---|
| Shipa_2022_2 [77] | R | 6 m | Clinical records | RA | 880 participants (655 in Cohort 1 and 225 in Cohort 2) |
| Shipa, 2023 [78] | R | 23.1 m | Clinical records | RA | 435 |
| Sieghart, 2018 [79] | P | 3–6 m | Clinical records | RA | 165 |
| Sonomoto, 2024 [80] | R | 6 m | FIRST registry | RA | 2223 |
| Strand, 2023 [81] | R | 7 m | CERTAIN study | RA | 143 |
| Sun, 2022 [82] | P | 36 m | Medical records | RA | 223 |
| Sundlisater, 2021 [83] | RCT | 12 m | ARCTIC REWIND | RA | 80 |
| Tao, 2021 [84] | P | 12 m | BiOCURA cohort | RA | 80 |
| Thomson, 2015 [85] | R | 14–16 m | Lab data | RA | 116 |
| Ukalovic, 2024 [86] | R | 6 m | BioReg | RA; SpA; PsA | 1397 |
| Valdivieso, 2024 [87] | R | 6 m | EMR | RA | 38 |
| Vauleon, 2018 [88] | R | 12 m | Clinical records | RA | 314 |
| Venerito_2022_2 [89] | R | 12 m | Clinical records | PsA | 119 |
| Venerito_2022_3 [90] | P | 24 m | EMR | RA | 367 |
| Venerito, 2024 [91] | R | Not mentioned | Clinical records and MRI | SpA | 32 |
| Verhavert, 2021 [92] | R | 8 w | CareRA | RA | 379 |
| Vodencarevic, 2020 [93] | P | 3 m | RETRO study | RA | 41 patients (135 follow-ups) |
| Vodencarevic, 2023 [94] | P | 16 w | AQUILA study | SpA | 580 |
| Wang, 2022 [95] | R | 12 w | RCT database | SpA | 1899 |
| Westerlind, 2021 [96] | R | 3 y | SRQ, NPR and PDR | RA | 5475 |
| Yap, 2024 [97] | R | 6 m | BRAGGSS | RA | 100 |
| Yoosuf, 2022 [98] | P | 3 m | COMBINE cohort | RA | 39 female patients |
| Zhang, 2023 [99] | R | 24w | GEO database (datasets GSE15316, GSE37107, and GSE54629) | RA | GSE15316: 9 samples GSE37107: 14 samples GSE54629: 68 samples |

*aTNF* tumour necrosis factor antagonists, *AS* ankylosis spondylitis; *BioReg* Austrian Registry for Biologicals, Biosimilars, and targeted synthetic, *BRAGGSS* Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate, *CareRA* care in rheumatoid arthritis trial, *CDAI* Clinical Disease Activity Index, *CT* clinical trial, *d* day, *DREAM* Dialogue on Reverse Engineering Assessment and Methods, *EAC* The Leiden Early Arthritis Clinic, *EIRA* Epidemiological Investigation of RA, *EMR* electronic medical record, *KOBIO* Korean College of Rheumatology Biologics, *KRRD* Kuwait Registry for Rheumatic Diseases, *m* month, *MA-RCT* meta-analysis of randomized controlled trials, *MATURA* Maximising Therapeutic Utility in Rheumatoid Arthritis, *NPR* National Patient Register, *lab* laboratory, *P* prospective study, *PAMERA* pharmacogenetics of methotrexate in rheumatoid arthritis, *PEAC* pathobiology of early arthritis cohort, *PDR* Prescribed Drug Register, *PsA* psoriatic arthritis, *R* retrospective study, *RA* rheumatoid arthritis, *RAMS* Rheumatoid Arthritis Medication Study, *RCT* randomized clinical trial, *REAPSER* Spanish Registry of Recent-onset Psoriatic Arthritis, *RISE* rheumatology informatics system for effectiveness, *SCQM* Swiss Clinical Quality Management in Rheumatic Diseases, *SpA* spondyloarthritis, *SRQ* Swedish Rheumatology Quality register, *TCZ* tocilizumab, *tREACH* treatment in the Rotterdam Early Arthritis CoHort, *tsDMARD* targeted synthetic disease-modifying antirheumatic drug, *UPOD* Utrecht Patient Oriented Database, *w* week, *y* year

of response often linked to baseline clinical characteristics, genetic markers, and disease activity scores. Tumour necrosis factor inhibitors (aTNF) were frequently evaluated, with predictive factors such as anti-citrullinated protein antibodies (ACPA) seropositivity, baseline C-reactive protein (CRP) levels, and clinical disease indices emerging as significant. Interleukin inhibitors, targeting IL-6, were analysed for predictors of response linked to biomarkers, imaging data, and molecular profiles. Janus kinase inhibitors (JAKi), such as tofacitinib and upadacitinib, showed predictive associations with genetic and proteomic factors, particularly in patients unresponsive to aTNF therapies. Other biologics, such as abatacept (ABA) and rituximab (RTX), revealed predictors like serological profiles and disease phenotypes influencing treatment outcomes. Studies frequently explored combinations of csDMARDs or tsDMARDs with biologics to identify clinical and molecular predictors of enhanced response. In Table S6 in the supplementary material we indicate the inclusion criteria of the included articles.

Table 2 also summarizes the data sources and outcomes evaluated in the included studies. The data utilized encompassed a wide range of types, including clinical information

such as disease activity scores, patient demographics, and treatment history; biomarker data, including genetic, proteomic, and transcriptomic profiles; and imaging data, such as ultrasound and MRI findings. The primary outcomes assessed were predictive factors of response to treatment, focusing on remission rates, persistence to therapy, and clinical improvement metrics, including DAS28 (Disease Activity Score in 28 Joints), CDAI (Clinical Disease Activity Index), and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index). The included studies employed a diverse range of ML techniques to predict treatment responses in RA, SpA, and PsA (see Table S7 for details). Supervised learning methods were the most applied, including regression models, Random Forest (RF), Support Vector Machines (SVM), and Gradient Boosting algorithms such as XGBoost and AdaBoost, which were frequently used for predicting remission, persistence, or non-response to treatment. Neural networks, including DL models, were implemented in some studies, particularly for complex datasets such as imaging or multi-omics profiles. Unsupervised learning methods, including clustering techniques like Uniform Manifold Approximation and Projection (UMAP) and hierarchical clustering, were used to uncover patient subgroups or patterns not evident through traditional analyses. Several studies also utilized specialized ML approaches such as LASSO (Least Absolute Shrinkage and Selection Operator) for feature selection, Shapley Additive Explanations (SHAP) for model interpretability, and Bayesian frameworks for probabilistic predictions. Predictors integrated into these models varied widely, including clinical features (e.g., baseline disease activity scores), biomarkers (e.g., genetic and proteomic profiles), and imaging data (e.g., ultrasound and MRI findings). Explainable AI (XAI) techniques, such as SHAP and Partial Dependence Plots, were increasingly applied to enhance the interpretability of complex models, ensuring their clinical relevance. To assess the degree of validation of each study, we included in the supplementary material (Table S8) whether each study performed internal and external validation. If validation was conducted, we also reported the method used.

Table 3 summarizes the main outcome measures used in the various predictive models and methodologies to identify RA and SpA treatment responses. It includes metrics such as accuracy, area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and odds ratios (OR). Only studies reporting results aligned with the specific metrics in each column are included in this table. Some studies used different ML models to obtain the results. In that case, different colours have been used to indicate which result corresponds to each model.

## Discussion

This ScR provides a comprehensive overview of the current landscape of AI applications in predicting treatment responses for RA and SpA. Our findings highlight the diverse and innovative ways AI/ML technologies are employed to enhance treatment prediction and personalization in rheumatology.

Our analysis revealed that most studies focused exclusively on RA, indicating a need for more research on AI/ML applications in SpA and PsA. The studies analysed various treatments, with MTX and aTNF being the most frequently evaluated. Our review revealed various AI and ML models utilized in rheumatology research, including RF algorithms, SVM and deep learning techniques. These models have been applied to various data types, including clinical records, genetic information, imaging data, and patient-reported outcomes. This diversity in AI approaches reflects the complexity of RA and SpA and the multifaceted nature of treatment response prediction.

One notable trend is the increasing use of multi-omics data and advanced imaging techniques in AI models. For instance, several studies incorporated genetic, proteomic and transcriptomic profiles alongside clinical data to enhance prediction accuracy. In this way, Tao et al. [84], demonstrated that integrating multi-omics data with clinical information significantly improved the prediction of treatment response in RA patients.

The diversity of data sources and outcomes evaluated across studies underscores AI's potential to leverage complex, heterogeneous datasets for personalized medicine in rheumatology. However, this diversity also challenges the standardization and generalizability of AI models across different patient populations and healthcare settings. Another relevant fact is that most of the studies included internal validation data, although work should continue on external validation (and their standardization). Regarding the data included, most included AUC, a range of variable values, mostly above 0.7, while the least reported values were PPV and NPV.

A key strength of this ScR is its comprehensive scope, encompassing a wide range of AI applications and treatment modalities in RA and SpA. However, several limitations must be acknowledged. First, the heterogeneity in study designs, AI methodologies, and outcome measures makes direct comparisons between studies challenging. Second, the predominance of retrospective studies (46 out of 89) highlights the need for more prospective validation of AI models in clinical settings. Finally, the limited number of studies on SpA and PsA compared to RA indicates a gap in the literature that future research should address (or a limitation of the strategy proposed by our side). The integration

**Table 2** Type of predictor, outcome and treatments used

| Study | Predictor Type | Outcome /Index | Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | csDMARDs | aTNF | anti-CTLA4 | IL6 | Anti CD20 | IL-17 | PDE4i | JAKi |
| Alsaber[11] | Clinical data | DAS28 | | | | | | | | |
| Aripova[12] | Biomarkers | EULAR response | | | | | | | | |
| Bai[13] | Biomarkers | SII | | | | | | | | |
| Bouget[14] | Clinical and biological data | EULAR response | | | | | | | | |
| Bouget_2022_3[15] | Clinical and biological data | EULAR response<br>DAS28 over time | | | | | | | | |
| Brizzi[16] | Biomarkers | DAS28 | | | | | | | | |
| Burkard[17] | Clinical data | ≥20% reduction in DAS28 | | | | | | | | |
| Casaburi[18] | Biomarkers | The need to switch to biological therapy | | | | | | | | |
| Chen[19] | Biomarkers | EULAR response | | | | | | | | |
| Cherlin[20] | Clinical data | Score CRP,<br>28 SJC score<br>ΔESR | | | | | | | | |
| Cho[21] | Biomarkers and clinical data | EULAR response | | | | | | | | |
| Cohen_2021_3[22] | Biomarkers and clinical data | ACR50<br>ACR70<br>DAS28-CRP | | | | | | | | |
| Curtis[23] | Biomarkers | CDAI | | | | | | | | |
| Dalen[24] | Clinical data | Treatment persistence | | | | | | | | |
| Dervieux[25] | Biomarkers and clinical data | EULAR response | | | | | | | | |
| Duong_2022_2[26] | Clinical data | DAS28-ESR | | | | | | | | |
| Duquesne[27] | Biomarkers and clinical data | EULAR response | | | | | | | | |
| Fadaei[28] | Clinical data | CDAI | | | | | | | | |
| Fernandez[29] | Clinical data | BASDAI50<br>ΔASDAS-CRP | | | | | | | | |
| Garcia-Dorta[30] | Clinical Data | Treatment retention | | | | | | | | |

**Table 2** (continued)

| Study | Predictor Type | Outcome /Index | Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | csDMARDs | aTNF | anti-CTLA4 | IL6 | Anti CD20 | IL-17 | PDE4i | JAKi |
| Gosselt[31] | Clinical data and biomarkers | DAS28 | | | | | | | | |
| Gottlieb[32] | Clinical data | ACR50/70<br>PASI 90<br>PASDAS-LDA<br>MDA | | | | | | | | |
| Guan[33] | Clinical and genetic data | DAS28 | | | | | | | | |
| Hageman[34] | Biomarkers | EULAR response | | | | | | | | |
| Icten[35] | Clinical data | CDAI | | | | | | | | |
| Jin[36] | Clinical data | Treatment changes | | | | | | | | |
| Johansson[37] | Clinical data | CDAI | | | | | | | | |
| Ju[38] | Genetic and clinical data | DAS28 | | | | | | | | |
| Kalweit[39] | Clinical data, PROs | DAS28 | | | | | | | | |
| Kato[40] | Imaging, biomarker | ACR20 | | | | | | | | |
| Kim_2021[41] | Genetic data | DAS28 | | | | | | | | |
| Kim_2023[42] | Genetic data | DAS28 | | | | | | | | |
| Kim_2024[43] | Clinical data | DAS28 | | | | | | | | |
| Kimpton[44] | Clinical data | Drug-survival | | | | | | | | |
| Koo[45] | Clinical data | DAS28 | | | | | | | | |
| Lee_2021_2[46] | Clinical data, PROs | ACR20<br>ASAS20 | | | | | | | | |
| Liede[47] | Clinical data | Treatment changes | | | | | | | | |
| Liede_2022_2[48] | Clinical data | Treatment changes | | | | | | | | |
| Lim[49] | Biomarkers and clinical data | DAS28 | | | | | | | | |
| Lim_2022_2[50] | Genetic and clinical data | DAS28 | | | | | | | | |
| Lopez-Pedrera[51] | Biomarkers and clinical data | DAS28 | | | | | | | | |
| Luque[52] | Biomarkers and clinical data | DAS28<br>SDAI<br>CDAI | | | | | | | | |

**Table 2** (continued)

| Study | Predictor Type | Outcome /Index | Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | csDMARDs | aTNF | anti-CTLA4 | IL6 | Anti CD20 | IL-17 | PDE4i | JAKi |
| Maarseveen[53] | Clinical data | Joint count | | | | | | | | |
| Maciejewski[54] | Biomarkers | EULAR response | | | | | | | | |
| Magrey[55] | Clinical data, PROs | ASDAS-CRP LDA | | | | | | | | |
| Matsuo[56] | Imaging, biomarkers | DAS28 | | | | | | | | |
| Mellors[57] | Biomarkers and clinical data | ACR50<br>ACR70 | | | | | | | | |
| Messelink[58] | Biomarkers, clinical data | DAS28 | | | | | | | | |
| Miyoshi[59] | Clinical data | DAS28 | | | | | | | | |
| Morid[60] | Other (administrative claims data) | Treatment change | | | | | | | | |
| Myasoedova[61] | Biomarkers, clinical data | EULAR response | | | | | | | | |
| Najm[62] | Biomarkers | CDAI | | | | | | | | |
| Nishimoto[63] | Genetic data | ACR70<br>EULAR response<br>IL6- normalization | | | | | | | | |
| Oberg Sysojev[64] | clinical data, demographics, medical history, genetic data | Treatment persistence | | | | | | | | |
| Perton[65] | Clinical data | MDA | | | | | | | | |
| Phillips[66] | Clinical data | Treatment change | | | | | | | | |
| Plant_2019_2[67] | Biomarkers | EULAR response | | | | | | | | |
| Prasad[68] | Biomarker/s, clinical data | DAS28 | | | | | | | | |
| Prenga[69] | Clinical data | DAS28 | | | | | | | | |
| Queiro[70] | Clinical data, PROs | MDA | | | | | | | | |
| Rehberg[71] | Biomarkers | DAS28 | | | | | | | | |
| Ritcher[72] | Clinical data | DAS28 | | | | | | | | |
| Rivellese[73] | Biomarkers | CDAI | | | | | | | | |
| Ruiz Romero[74] | Biomarkers | EULAR response | | | | | | | | |
| Salehi[75] | Clinical data | DAS28 | | | | | | | | |

**Table 2** (continued)

| Study | Predictor Type | Outcome /Index | Treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | csDMARDs | aTNF | anti-CTLA4 | IL6 | Anti CD20 | IL-17 | PDE4i | JAKi |
| Shipa[76] | Biomarker/s, imaging, clinical data, PROs | Treatment persistence | | | | | | | | |
| Shipa_2022_2[77] | Biomarker | DAS28 | | | | | | | | |
| Shipa_2023[78] | Clinical data | Treatment persistence | | | | | | | | |
| Sieghart[79] | Biomarkers | ACR20 | | | | | | | | |
| Sonomoto[80] | Clinical data, PRO | CDAI | | | | | | | | |
| Strand[81] | Clinical data | ACR50 | | | | | | | | |
| Sun[82] | Biomarkers, clinical data, PROs | DAS28 | | | | | | | | |
| Sundlisater[83] | Clinical, and US data | DAS44 | | | | | | | | |
| Tao[84] | Biomarkers | EULAR response | | | | | | | | |
| Thomson[85] | Biomarker/s | EULAR response | | | | | | | | |
| Ukalovic[86] | Clinical data | Treatment persistence | | | | | | | | |
| Valdivieso[87] | Biomarker/s and clinical data | DAS28 | | | | | | | | |
| Vauleon[88] | Clinical data | Treatment persistence | | | | | | | | |
| Venerito_2022_2[89] | Biomarkers and clinical data | DAPSA | | | | | | | | |
| Venerito_2022_3[90] | Clinical data, PROs | DAS28 | | | | | | | | |
| Venerito[91] | Clinical and radiological data | Treatment persistence | | | | | | | | |
| Verhavert[92] | Clinical data | DAS28 | | | | | | | | |
| Vodencarevic[93] | Clinical data | Treatment persistence | | | | | | | | |
| Vodencarevic[94] | Clinical data | LDA | | | | | | | | |
| Wang[95] | Clinical data, PROs | ASDAS | | | | | | | | |
| Westerlind[96] | Clinical data | Treatment persistence | | | | | | | | |
| Yap[97] | Biomarkers | EULAR response | | | | | | | | |
| Yoosuf[98] | Biomarkers, clinical data, | EULAR response | | | | | | | | |
| Zhang[99] | Biomarkers | DAS28 | | | | | | | | |

*ABA* abatacept, *ACPA* anti-citrullinated peptide antibodies, *ADA* adalimumab, *AUC* area under the curve, *ASDAS* Axial Spondyloarthritis Disease Activity Score, *aTNF* tumour necrosis factor inhibitors, *AUROC* area under the receiver operating characteristic curve, *AS* ankylosis spondylitis, *bDMARDs* biologic disease-modifying antirheumatic drug, *BMI* body mass index, *CDAI* Clinical Disease Activity Index, *CERTO* certolizumab pegol, *CI* confidence interval, *CRP* C-reactive protein, *csDMARDs* conventional Disease-modifying Antirheumatic Drug, *CV* cardiovascular, *DAS28* Disease Activity Score, *ETN* etanercept, *ESR* erythrocyte sedimentation rate, *GOL* golimumab, *IFX* Infliximab, *HR* hazard ratio, *LASSO* least absolute shrinkage and selection operator, *LDA* low disease activity, *LEF* leflunomide, *m* months, *MBI* much better improvement, *MDA* minimal disease activity, *MDR* multifactor dimensionality reduction, *ML* machine learning, *MTX* methotrexate, *NPV* negative predictive value, *NSAIDs* non-steroidal anti-inflammatory drugs, *OR* odds ratio, *PASI* Psoriasis Area and Severity Index, *PC* principal components, *PPV* positive predictive value, *PsA* psoriatic arthritis, *RA* rheumatoid arthritis, *RF* rheumatoid factor, *SARI* sarilumab, *SDAI* Simplified Disease Activity Index, *SHAP* shapley additive explanation, *SII* systemic immune inflammation, *SJC* swollen joint count, *SpA* spondyloarthritis, *SVM* support vector machine, *TCZ* tocilizumab, *TJC* tender joint counts, *TOF* tofacitinib, *tsDMARD* targeted synthetic disease-modifying Antirheumatic drug, *UMAP* unsupervised machine learning, *w* week

**Table 3** Main results of the outcome measures used

| Outcome | AUC | Se / Sp | Other measures of performance | | Studies |
|---|---|---|---|---|---|
| **DAS28** | .46 to .72 | | Accuracy | .53 to .73 | Alsaber[11] |
| | .76 (.71 to .81)<br>.96 (.94 to .98) | .73 / .66<br>.97 / .96 | Accuracy<br>PPV/NPV | .96<br>.72 / .67<br>.97 / .96 | Duong_2022_2[26] |
| | .76 (.67 to .85)<br>.71 (.61 to .81)<br>.77 (.68 to .86)<br>.70 (.61 to .81) | .81 / Null | | | Gosselt[31] |
| | .64<br>.64<br>.65<br>.65<br>.64 | | | | Guan[33] |
| | .63 to .67 | | | | Ju[38] |
| | .70 (.58 to .82)<br>.71 (.59 to .83)<br>.60 (.42 to .78)[1]<br>.67 (.53 to .81)[2] | | | | Kim_2021[41] |
| | .64 (.52 to .75)<br>.65 (.53 to .76)<br>.60 (.46 to .74)[2]<br>.65 (.54 to .76) | | | | Kim_2023[42] |
| | .76 | | | | Kim_2024[43] |
| | .53 to .73 | .51 to .69 / Null | | | Koo[45] |
| | .78 to .83 | .66 to 81.3 / 68.4 to 86.8 | | | Lim[49] |
| | .75 to .96 | 58.1 to 91.5 / 64.1 to 92.3 | | | Lim_2022_2[50] |
| | .855 to .92 | 71.5 to 89.2 / 73.3 to 86.2 | | | Lopez to Pedreda[51] |
| | .68<br>.65<br>.66 | | | | Matsuo[56] |
| | .73 (.71 to .75) | .69 / .92<br>.79 / .50 | | | Messelink[58] |
| | .75 | .97 / .75 | Accuracy | .92 | Miyoshi[59] |
| | | .75 / .86 | | | Prasad[68] |
| | .60 to .87 | .61 to .99 / .10 to .76 | | | Prenga[69] |
| | .74[3]<br>.68[4] | | | | Rivellese[73] |
| | .91<br>.91<br>.85<br>.83<br>.85 | | Accuracy | .85<br>.85<br>.81<br>.76<br>.80 | Salehi[75] |
| | >.70 | 90 / 70 | OR<br>Accuracy | 16.2 (5.7 to 46.4)<br>.81 (.76 to .86) | Shipa_2022_2[77] |
| | .76[3]<br>.82[4]<br>.73[5] | | | | Sun[82] |
| | .80 to .89 | | Accuracy | .79 to .90 | Valdivieso[87] |
| | .72<br>.71<br>.75<br>.63 | | Accuracy | .65<br>.66<br>.73<br>.62 | Venerito_2022_3[90] |
| | .70[6]<br>.89[7] | | | | Zhang[99] |
| **DAS28 LDA** | .69[3]<br>.67[4] | | OR | 4.1 (1.9 to 9.1)[3]<br>3.6 (1.8 to 7.3)[4] | Cohen_2021_3[22] |
| **DAS28 remission** | .60[3]<br>.73[4] | | OR | 1.4 (0.6 to 3.1)[3]<br>5.8 (2.6 to 13.0)[4] | Cohen_2021_3[22] |
| **EULAR response** | | | OR | 1.76 (1.22 to 2.53)<br>1.74 (1.23 to 2.46) | Aripova[12] |
| | .72 (.70 to .73) | | | | Bouget[14] |
| | .72 (.68 to .73) | | | | Bouget_2022_2[15] |
| | .72[8]<br>.85[9]<br>.79[10] | | | | Chen [19] |
| | .84 | 1.00 / .60 | | | Cho[21] |

**Table 3** (continued)

| Outcome | AUC | Se / Sp | Other measures of performance | | Studies |
|---|---|---|---|---|---|
| | | | OR | 2.18 (1.64 to 2.90) | Dervieux[25] |
| | .72 | .90 / .38 | Accuracy<br>PPV / NPV | .74<br>.77 / .62 | Duquesne[27] |
| | .76 | | | | Hageman[34] |
| | .61 | | | | Maciejewski[54] |
| | .84 | .72 / .77 | | | Myasoedova[3] |
| | | .97 / .83 | PPV / NPV | .86 / .71 | Nishimoto[63] |
| | .78 | | Accuracy | .61 | Plant_2019_2[67] |
| | | .88 / 1.00 | PPV / NPV | 1.00 / .88 | Ruiz Romero [74] |
| | | | Accuracy | .86[Error! Bookmark not defined.]<br>.79[11] | Tao[84] |
| | .71 (.60 to .81) | .31 / .92 | Accuracy | .60 | Thomson[85] |
| | .86<br>.82[5] | | | | Yap[97] |
| **Treatment change** | .85 | .92 / .69 | | | Casaburi[18] |
| | | | OR | 3.33 (1.83 to 6.09) | Phillips[66] |
| | .64[12] | | | | Jin[36] |
| **ACR20** | .64<br>.60<br>.60<br>.63 | | Accuracy | .75<br>.75<br>.75<br>.74 | Lee_2021_2[46] |
| **ACR50** | .67[3]<br>.64[4] | | | 3.7 (1.7 to 8.0)[3]<br>4.1 (2.0 to 8.3)[4] | Cohen_2021_3[22] |
| | | | | 24.70 (20.22 to 29.19)[13]<br>20.19 (16.04 to 24.16)[14]<br>16.64 (12.07 to 21.78)[15] | Gottlieb[32] |
| | | .87 / .50 | OR<br>PPV / NPV | 6.57<br>.90 / Null | Mellors[57] |
| | .65[16]<br>.60[17]<br>.41[18] | | | | Strand[81] |
| **ACR70** | .66[3]<br>.70[4] | | | 2.5 (1.0 to 6.2)[3]<br>6.7 (2.7 to 16.7)[4] | Cohen_2021_3[22] |
| | | | | 13.16 (9.54 to 16.79)[13]<br>9.27 (6.40 to 11.99)[14]<br>8.35 (5.17 to 11.92)[15] | Gottlieb[32] |
| | | Null / .84 | PPV / NPV | .94 / Null | Mellors[57] |
| | | .73 / .97 | PPV / NPV | .50 / .84 | Nishimoto[63] |
| **CDAI** | | | OR | 1.5 (0.7 to 3.2) | Curtis[23] |
| | | | OR | 1.02 (0.98 to 1.06) | Fadaei[28] |
| | .76<br>.72 | Null / .66 | Accuracy | .71 | Icten[35] |
| | | | OR | 0.69 (0.62 to 0.75) | Johansson[37] |
| | .88 | .78 / .79 | | | Najm[62] |
| | .70 | .62 / .70 | PPV / NPV | .53 / .74 | Sonomoto[80] |
| **CDAI to LDA** | .65[3]<br>.68[4] | | OR | 3.4 (1.6 to 7.0)[3]<br>3.6 (1.8 to 7.2)[4] | Cohen_2021_3[22] |
| **CDAI-Remission** | .70[3]<br>.74[4] | | OR | 2.6 (1.1 to 6.1)[3]<br>8.8 (2.9 to 27.3)[4] | Cohen_2021_3[22] |
| **Treatment persistence** | .74 | | Accuracy<br>PPV / NPV | .77<br>.83 / .57 | García to Dorta[30] |
| | | | HR | 0.57 (0.33 to 0.98) | Kimptom[44] |
| | .56 | | | | Liede[47] |
| | .62 | | | | Liede_2021_2[48] |
| | .62 | | | | Oberg Sysojev[64] |
| | | | HR | 0.49 (0.32 to 0.75)[19]<br>0.49 (0.33 to 0.72)[20]<br>0.42 (0.20 to 0.87)[21]<br>0.55 (0.34 to 0.88)[22] | Shipa[78] |
| | | | HR | 0.63 (0.48 to 0.83)[23] | Shipa_2023[78] |

**Table 3** (continued)

| Outcome | AUC | Se / Sp | Other measures of performance | | Studies |
|---|---|---|---|---|---|
| | | | | 0.52 (0.38 to 0.73)[24]<br>0.59 (0.42 to 0.85)[25]<br>1.04 (0.63 to 1.73)[26] | |
| | .66 (.54 to .78)[27]<br>.70 (.68 to .74)Error! Bookmark not defined.<br>.84 (.79 to .89)[28]<br>.68 (.55 to .87)[11]<br>.72 (.69 to .77)Error! Bookmark not defined. | | | | Ukalovic[86] |
| | | | HR | 2.10 (1.09 to 4.05) | Venerito_2024[91] |
| | .80 (.72 to .89) | | | | Vodencarevic[93] |
| **ASDAS-CRP** | | | OR | 2.11 (0.83 to 5.37) | Magrey[55] |
| | .65 to .81 | Moderate / High | PPV / NPV | .49 to .77 / .81 to .84 | Wang[95] |
| **ASAS20** | .66<br>.64<br>.60<br>.63<br>.61 | | Accuracy | .67<br>.67<br>.64<br>.65<br>.64 | Lee_2021_2[46] |
| **PASI90** | | | OR | 41.04 (33.11 to 49.26)[13]<br>29.10 (22.47 to 34.89)[14]<br>18.21 (11.70 to 25.94)[15] | Gottlieb[32] |
| **PASDAS** | | | OR | 27.88 (22.84 to 33.19)[13]<br>18.52 (14.24 to 22.68)[14]<br>19.61 (14.68 to 25.80)[15] | Gottlieb[32] |
| **MDA or LDA** | | | OR | 17.19 (13.19 to 21.47)[13]<br>12.77 (9.25 to 16.10)[14]<br>9.24 (5.74 to 12.78)[15] | Gottlieb[32] |
| | .79 | | | | Perton[65] |
| | .84 | .87 / .67 | | | Vodencarevic[93] |
| **Joint Count** | | | HR | 0.5 (0.36 to 0.7) | Maarseveen[53] |
| **IL6 normalisation** | | .96 / .91 | .92 / .73 | | Nishimoto[63] |
| **DAPSA** | .97<br>.78 | | Accuracy | .97<br>.73 | Venerito_2022_2[89] |

*DAS28* disease activity score, *AUC* area under curve, *Se* sensitivity, *Sp* specificity, *PPV* positive predictive value, *NPV* negative predictive value, *OR* odds ratio, *HR* hazard ratio, *csDMARDs* conventional synthetic disease-modifying antirheumatic drugs, *pred* prednisone, *TCZ* tocilizumab, *ADA* adalimumab, *RF* rheumatoid factor, *SII* systemic inflammation index, *CRP* C-reactive protein, *MDA* minimal disease activity, *LDA* low disease

When articles reported results using different machine learning models, we used the following colour code:
LASSO
Random Forest
Logistic regression
XGBoost
Gaussian process regression
SVM
Elastic net
Knn
AdaBoost
[1]Linear
[2]Radial
[3]3 Months

[4]6 months
[5]12 months
[6]BANK1
[7]SNX6
[8]FGB
[9]HEL-S-282
[10]A0A140VJJ6
[11]Etanercept
[12]C-statistic
[13]Secukinumab 300 mg
[14]Secukinumab 150 mg
[15]Secukinumab 150 mg (no load)
[16]Molecular and clinical features
[17]Molecular features only
[18]Clinical features only
[19]Adalimumab vs etanercept
[20]AntiTNF monotherapy *vs* antiTNF + MTX
[21]Adalimumab monotherapy *vs* adalimumab + MTX
[22]Etanercept monotherapy *vs* etanercept + MTX
[23]Biologic of different mode of action *vs* second antiTNF
[24]Biologic of different mode of action *vs* second antiTNF in seropositive RA (either RF or ACPA)
[25]Biologic of different mode of action *vs* second antiTNF in seropositive RA (both RF and ACPA)
[26]Biologic of different mode of action *vs* second antiTNF in seronegative RA
[27]Abatacept
[28]Certolizumab

of AI technologies in rheumatology offers the potential to enhance personalized care significantly. By tailoring treatment plans based on individual patient profiles, clinicians may achieve better outcomes and reduce the trial-and-error approach currently common in RA and SpA management. The combination of AI and pharmacogenomics, as demonstrated in studies predicting patient responses to specific RA treatments like MTX, represents a promising avenue for personalized medicine in rheumatology.

To unlock the full potential of AI in rheumatology, future studies should focus more on integrating knowledge, ensuring that insights generated by AI are effectively incorporated into clinical decision-making. A key strategy is standardising data collection and model validation, allowing for comparability across different studies and facilitating meta-analyses. Developing explainable AI (XAI) models will also be crucial for enhancing transparency and building clinician trust, making AI-driven predictions more interpretable and actionable.

Further research should emphasize prospective, multicenter studies with diverse patient populations to improve generalizability and external validation. Integrating multi-omics data, real-world evidence, and patient-reported outcomes will also be vital for refining predictive models (Table 4).

Moreover, interdisciplinary collaboration among rheumatologists, data scientists, and regulatory bodies is necessary to establish guidelines for clinical implementation. Finally, efforts should focus on incorporating AI tools into electronic health records and clinical workflows to ensure seamless adoption and real-time utility in patient management. By addressing these areas, future research can bridge the gap between AI innovation and its practical application in rheumatology, ultimately enhancing personalized treatment strategies for RA and SpA.

In conclusion, while AI shows significant promise in enhancing treatment prediction and personalization in RA and SpA, continued research is essential to address current limitations and fully realize its potential in improving patient outcomes. The field of rheumatology stands at the cusp of a technological revolution, and the judicious integration of AI technologies may lead to more precise, effective, and personalized care for patients with RA and SpA.

**Table 4** Main results of the outcome measures used

| Index | Accuracy | AUC | Sensitivity % | Specificity % | PPV % | NPV % | OR | Study |
|---|---|---|---|---|---|---|---|---|
| DAS28 | 52.8 - 72.9 | 0.463-0.719 | | | | | | Alsaber[11] |
| | | | | | | | 5.46 (1.76–16.94)[21*] 8.44 (3.43–20.74[4*] 3.64 (2.04–6.49)[15*] | Burkard[17] |
| | 96 | 0.76 (0.71, 0.81) 0.96 (0.94, 0.98) | 0.73 0.97 | 0.66 0.96 | 0.72 0.97 | 0.67 0.96 | | Duong_2022_2[26] |
| | | 0.76 (0.67–0.85) 0.71(0.61-0.81) 0.77 (0.68–0.86) 0.70(0.61–0.81) | 0.81 | | | | | Gosselt[31] |
| | | 0.638 0.636 0.652 0.653 0.639 | | | | | | Guan[33] |
| | | 0.63 to 0.67 | | | | | | Ju[38] |
| | | | | | | | 5.46 (1.76-16.94)[21*] 8.44 (3.43-20.74)[22*] | Kalweit[39] |
| | | 0.70 (0.584-0.821) 0.71 (0.594-0.827) 0.60 (0.416-0.782)[1] 0.67 (0.53-0.81)[2] | | | | | | Kim_2021[41] |
| | | 0.64 (0.52-0.75) 0.65 (0.53-0.76) 0.60 (0.46-0.74)[2] 0.65 (0.54-0.76) | | | | | | Kim_2023[42] |
| | | 0.762 | | | | | | Kim_2024[43] |
| | | 52.8-72.9 | 51.1-69.4 | | | | | Koo[45] |
| | | 0.776-0.828 | 65.6-81.3 | 68.4-86.8 | | | | Lim[49] |
| | | 0.751-0.959 | 58.1-91.5 | 64.1-92.3 | | | | Lim_2022_2[50] |
| | | 0.855 to 0.916 | 71.5 to 89.2 | 73.3 to 86.2 | | | | Lopez-Pedreda[51] |
| | | 0.677 0.645 | | | | | | Matsuo[56] |

**Table 4** (continued)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 0.664 | | | | | | |
| | | 0.73 (0.71-0.75) | 69<br>79 | 92<br>50 | | | | Messelink[58] |
| | 92 | 0.75 | 96.7 | 75 | | | | Miyoshi[59] |
| | | | 75 | 86 | | | | Prasad[68] |
| | | 0.60-0.87 | 61-99 | 10-76 | | | | Prenga[69] |
| | | 0.744[3]<br>0.681[4] | | | | | | Rivellese[73] |
| | 85<br>85<br>81<br>76<br>80 | 0.908<br>(0.065)<br>0.910<br>(0.040)<br>0.848<br>(0.034)<br>0.827<br>(0.081)<br>0.849<br>(0.060) | | | | | | Salehi[75] |
| | 81 (76-86), | >0.70 | 90, | 70, | | | 16.2 (5.7-46.4) | Shipa_2022_2[77] |
| | | 0.76[5]<br>0.82[6]<br>0.73 [7] | | | | | | Sun[82] |
| | 78.9 to 89.6 | 0.804 to 0.891 | | | | | | Valdivieso[87] |
| | 64.9<br>65.9<br>72.7<br>62.3 | 0.72<br>0.71<br>0.75<br>0.63 | | | | | | Venerito_2022_3[90] |
| | | | | | | | 0.75 (0.69-0.82)*<br>0.76 (0.68-0.80)* | Verhavert[92] |
| | | 0.704[8]<br>0.886[9] | | | | | | Zhang[99] |
| DAS28 LDA | | 0.69 [5]<br>0.67[6] | | | | | 4.1 (1.9-9.1)[5]<br>3.6 (1.8-7.3)[6] | Cohen_2021_3[22] |
| DAS28 remission | | 0.60[5]<br>0.73[6] | | | | | 1.4 (0.6-3.1)[5]<br>5.8 (2.6-13.0)[6] | Cohen_2021_3[22] |
| EULAR response | | | | | | | 1 .76; (1 .22-2.53)<br>1 .74 (1 .23-2.46) | Aripova[12] |
| | | 0.72 (0.70-0.73) | | | | | | Bouget[14] |
| | | 0.72 (0.68-0.73) | | | | | | Bouget_2022_2[15] |
| | | 0.720[12]<br>0.853[13]<br>0.787[14] | | | | | | Chen [19] |
| | | 0.84 | 100 | 60 | | | | Cho[21] |
| | | | | | | | 2.18 (1.64–2.90) | Dervieux[25] |
| | 74 | 0.72 | 90 | 38 | 77 | 62 | | Duquesne[27] |
| | | 0.76 | | | | | | Hageman[34] |
| | | 0.61 ± 0.02 | | | | | | Maciejewski[54] |
| | | 0.84 | 72 | 77 | | | | Myasoedova[3] |
| | | | 97 | 83 | 86 | 71 | | Nishimoto[63] |
| | 61 | 0.78 ± 0.11 | | | | | | Plant_2019_2[67] |
| | | | 88 | 100 | 100 | 88 | | Ruiz Romero [74] |
| | 85.9 [15]<br>ETN:79[16] | | | | | | | Tao[84] |

**Table 4** (continued)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 60 | 0.71 (0.60-0.81) | 31 | 92 | | | | Thomson[85] |
| | | 0.86 ± 0.13 0.82 ± 0.15[5] | | | | | | Yap[97] |
| Neutrophil Count | | 0.668 (0.564-0.771) | 87.71 | 40.63 | | | | Bai[13] |
| Lymphocyte Count | | 0.869 (0.811-0.928) | 77.87 | 84.38 | | | | Bai[13] |
| Platelet Count | | 0.891 (0.838-0.945) | 81.97 | 87.50 | | | | Bai [13] |
| SII Index | | 0.708 (0.594-0.822) | | | | | | Bai[13] |
| CRP | | 0.678 (0.555-0.800) | | | | | | Bai [13] |
| RF | | 0.725 (0.619-0.831) | | | | | | Bai [13] |
| Treatment change | | 0.85 | 92 | 69 | | | | Casaburi[18] |
| | | | | | | | 3.33 (1.83-6.09) | Phillips[66] |
| | | 0.64* | | | | | | Jin[36] |
| ACR20 | 74.6<br>74.6<br>74.6<br>73.5 | 0.642<br>0.597<br>0.598<br>0.629 | | | | | | Lee_2021_2[46] |
| ACR50 | | 0.67 [5]<br>0.64 [6] | | | | | 3.7 (1.7-8.0)[5]<br>4.1 (2.0-8.3)[6] | Cohen_2021_3[22] |
| | | | | | | | 24.70(20.22-29.19)[17.1]<br>20.19 (16.04-24.16)[17.2]<br>16.64 (12.07-21.78)[17.3] | Gottlieb[32] |
| | | | 86.8 | 50.0 | 89.7 | | 6.57 | Mellors[57] |
| | | 0.65[18]<br>0.60[18.1]<br>0.41[18.2] | | | | | | Strand[81] |
| ACR70 | | 0.66 [5]<br>0.70[6] | | | | | 2.5 (1.0-6.2)[5]<br>6.7 (2.7-16.7)[6] | Cohen_2021_3[22] |
| | | | | | | | 13.16 (9.54-16.79)[17.1]<br>9.27 (6.40-11.99)[17.2]<br>8.35 (5.17-11.92)[17.3] | Gottlieb[32] |
| | | | | 84.4 | 93.5 | | | Mellors[57] |
| | | | 73 | 97 | 50 | 84 | | Nishimoto[63] |
| CDAI | | | | | | | 1.5 (0.7-3.2) | Curtis[23] |
| | | | | | | | 1.02 (0.98-1.06) | Fadaei[28] |
| | 70.9 | 0.764<br>0.723 | | 65.5 | | | | Icten[35] |
| | | | | | | | 0.69 (0.62–0.75) | Johansson[37] |

**Table 4** (continued)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 0.88 | 78 | 78.6 | | | | Najm[62] |
| | | 0.704 | 61.7 | 69.9 | 53.2 | 73.6 | | Sonomoto[80] |
| CDAI-LDA | | 0.65 [5]<br>0.68[6] | | | | | 3.4 (1.6-7.0)[5]<br>3.6 (1.8-7.2)[6] | Cohen_2021_3[22] |
| CDAI-Remission | | 0.70[5]<br>0.74 [6] | | | | | 2.6 (1.1-6.1)[5]<br>8.8 (2.9-27.3)[6] | Cohen_2021_3[22] |
| Treatment persistence | 77.2 | 0.743 | | | 83.1 | 57.1 | | García-Dorta[30] |
| | | | | | | | 0.57 (0.33-0.98)* | Kimptom[44] |
| | | 0.56 | | | | | | Liede[47] |
| | | 0.624 | | | | | | Liede_2021_2[48] |
| | | 0.62 | | | | | | Oberg Sysojev[64] |
| | | | | | | | 0.49 (0.32-0.75)[15vs 16*]<br>aTNF monotherapy vs TNFa-MTX: 0.49 (0.33-0.72)*<br>ADA monotherapy vs ADA-MTX combination: 0.42 (0.20-0.87)*<br>ETN monotherapy vs ETN-MTX combination: 0.55 (0.34-0.88)* | Shipa[78] |
| | | | | | | | Biologic of different mode of action vs Second TNFa: 0.63 (0.48-0.83)*<br>Biologic of different mode of action vs Second TNFa in seropositive RA (either RF or ACPA): 0.52 (0.38-0.73)*<br>Biologic of different mode of action vs Second TNFa in seropositive RA (both RF or ACPA):0.59 (0.42-0.85)*<br>Biologic of different mode of action vs Second TNFa in | Shipa_2023[78] |

**Table 4** (continued)

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | seronegative RA: 1.04 (0.63-1.73)* | |
| | | 0.66 (0.54-0.78)[19] 0.70 (0.68-0.74)[15] 0.84 (0.79-0.89)[20] 0.68 (0.55-0.87)[16] 0.72 (0.69-0.77) [4] | | | | | | Ukalovic[86] |
| | | | | | | | 2.10 (1.09-4.05)* | Venerito_2024[91] |
| | | 0.80 (0.72 – 0.89) | | | | | | Vodencarevic[93] |
| ASDAS-CRP | | | | | | | 2.11 (0.83-5.37) | Magrey[55] |
| | | 0.65 to 0.81 | Moderate | High | 49 to 77 | 81 to 84 | | Wang[95] |
| ASAS20 | 67 66.9 64.3 64.8 64.4 | 0.655 0.636 0.601 0.629 0.613 | | | | | | Lee_2021_2[46] |
| PASI90 | | | | | | | 41.04 (33.11-49.26)[17.1] 29.10 (22.47-34.89)[17.2] 18.21 (11.70-25.94)[17.3] | Gottlieb[32] |
| PASDAS | | | | | | | 27.88 (22.84-33.19)[17.1] 18.52 (14.24-22.68)[17.2] 19.61 (14.68-25.80)[17.3] | Gottlieb[32] |
| MDA or LDA | | | | | | | 17.19 (13.19-21.47)[17.1] 12.77 (9.25-16.10)[17.2] 9.24 (5.74-12.78)[17.3] | Gottlieb[32] |
| | | 0.788 | | | | | | Perton[65] |
| | | 0.84 | 87 | 67 | | | | Vodencarevic[93] |
| Joint Count | | | | | | | 0.5 (0.36-0.7)* | Maarseveen[53] |
| IL6 normalization | | | 96 | 91 | 92 | 73 | | Nishimoto[63] |
| DAPSA | 97 73 | 0.97 0.78 | | | | | | Venerito_2022_2[89] |

*DAS28* disease activity index, *AUC* area under curve, *PPV* positive predictive value, *NPV* negative predictive value, *OR* odds ratio, *HR* hazard ratio, *csDMARDs* conventional disease-modifying antirheumatic drugs, *pred* prednisone, *TCZ* tocilizumab, *ADA* adalimumab, *RF* rheumatoid

factor, *SII* systemic immune-inflammation index, *CRP* C-reactive protein, *MDA* minimal disease activity, *LDA* low disease activity, ACR

Superscripts: 1. Linear; 2. Radial; 3. Rituximab; 4. Tocilizumab; 5. 3 Months; 6. 6 months; 7. 12 months; 8. BANK1; 9. SNX6; 10. ACPA ≤ 1 5; 11. ACPA16-250; 12. FGB; 13. HEL-S-282; 14. A0A140VJJ6; 15. Adalimumab; 16. Etanercept; 17.1 Secukinumab300mg; 17.2 Secukinumab150mg; 17.3 Secukinumab150mg (no load); 18. Molecular and clinical features; 18.1 Molecular features; 18.2 Clinical features; 19. Abatacept; 20. Certolizumab; 21. ≥ 2 csDMARDs + pred; 22. Male

*In the AUC column it means it is a c-statistic, and in the OR column, it means HR

**Multiple different clusters were used to perform the analyses, with quite similar results

When articles reported results using different machine learning models, we used the following colour code:

- LASSO
- Random Forest
- Logistic regression
- XGBoost
- Gaussian process regression
- SVM
- Elastic net
- Knn
- AdaBoost

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**Data availability** Data available on request.

## Declarations

**Conflict of interest** Diego Benavent, Jose Francisco García Llorente, and Antonio Gómez-Centeno were paid consultants to Pfizer for their involvement in developing this manuscript and on the steering committee. Loreto Carmona, Teresa Otón, and Estíbaliz Loza are employees of INMUSC, which Pfizer contracted to conduct and supervise the review. Maria Montoro and Susan Ramirez are Pfizer employees.



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