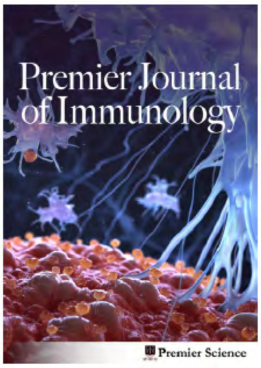
PREMIER JOURNAL OF IMMUNOLOGY REVIEW



Application of Machine Learning in Autoimmune Diseases: A Review of Current Trends and Future Prospects

Sumit Sharma

[1]Institute of Molecular Biology and Biotechnology, Bahauddin [2]Zakariya University, Multan, Pakistan

Correspondence to: Sumit Sharma, drsumits@outlook.com

Additional material is published online only. To view please visit the journal online.

Cite this as: Sharma S. Application of Machine Learning in Autoimmune Diseases: A Review of Current Trends and Future Prospects. Premier Journal of Immunology 2026;5:100009

DOI: https://doi.org/10.70389/PJI.100009

Received: xx xxxx xxxx

Revised: 1 March 2026

Accepted: 1 March 2026

Version accepted: 3

Published: xx xxxxx xxxx

Ethical approval: N/a

Consent: N/a

Funding: No industry funding

Conflicts of interest: N/a

Author contribution: Sumit Sharma – Conceptualization, Writing – review and editing

Guarantor: Dr Sumit Sharma, Research Scientist, Nutralytics Edtech LLP, Pune, India

Provenance and peer-review: N/a

ABSTRACT

Autoimmune diseases are among the primary global healthcare burdens, with a prevalence of 5%–10%, and are more prevalent in women and older patients. Currently, diagnosis is based on serological markers such as autoantibodies, inflammatory markers, radiological imaging, and clinical scoring systems and hence lacks a substantial biomarker-based diagnosis. Similarly, treatment paradigms differ significantly across centers, and treatment decisions are made based on a "one-size-fits-all" approach, leading to compromised clinical outcomes. Artificial intelligence (AI) and machine learning (ML) have emerged as transformative tools in the diagnosis and management of autoimmune disease. The AI/ML works on multimodal datasets or multiomic models, integrating data from genomics, proteomics, laboratory reports, electronic health records (EHRs), and patient-reported outcomes (PROs) to achieve early diagnosis, safe and effective management, and improved quality of life for patients. AI/ML also plays a pivotal role in personalized medicine, flare prediction, risk stratification, and drug discovery for autoimmune disease. Hence, in the current manuscript, we have discussed the role of AI/ML in various autoimmune diseases, the emerging role in personalized medicine and drug discovery, and the upcoming role in clinical trials. Notably, we also emphasized the challenges of such data and privacy protection, ethical and regulatory considerations, and the road map for the future. Hence, this review provides an overview of current trends and the future role of AI/ML in autoimmune disease and will support biomedical scientists, researchers, and AI scientists in harnessing AI/ML for next-generation, data-driven autoimmune care.

Keywords: Deep learning; Diagnosis; Biomarker; Random forests and clinical outcome

Introduction

Autoimmune disease ranks third globally in terms of its prevalence, after cancer and cardiovascular disorders.[1] Also, as per the published evidence, 5%–10% of the global population is affected by autoimmune disease, with prevalence in women being more common.[1] According to a 2021 study, psoriasis had the highest age-standardized incidence rate among individuals >60 years of age, followed by rheumatoid arthritis (RA), inflammatory bowel disease (IBD), type 1 diabetes mellitus (T1DM), and multiple sclerosis (MS).[1] Notably, the socio-demographic index for the population >60 years showed RA as the most prevalent, followed by IBD, T1DM, and psoriasis. Hence, it can be concluded that RA and psoriasis are common in most autoimmune diseases, followed by an increase in the prevalence of T1DM.[1] However, there has been a decline in mortality, confirming the advances in the diagnosis and treatment of autoimmune disease. Considering the pathogenesis of autoimmune disease, environmental factors, genetic factors, dysregulated immune system, etc., contribute in common. Also, there has been a positive correlation between human leukocyte antigen-DR4 and RA; HLA-DR3/DR4 and T1DM; Epstein–Barr virus and cytomegalovirus and MS; and systemic lupus erythematosus (SLE) and interleukin-23 (IL-23). Despite the improvement in diagnostic approach, autoimmune disease is challenging, and most of the time, there is misdiagnosis because of overlapping and non-specific symptoms. Commonly used biomarkers, such as autoantibodies and inflammation markers, along with clinical criteria, failed to distinguish between autoimmune disease and other diseases.[2] Standard treatment approaches include non-steroidal anti-inflammatory drugs, corticosteroids, disease-modifying antirheumatic drugs, and inhibitors of interleukin-6 (IL-6) and tumor necrosis factor-alpha. These treatment approaches indeed slow down the damage or control the symptoms but are also associated with severe side effects, such as GI toxicities, osteoporosis, and adrenal suppression.[3] Also, the treatment and related modalities do not address the primary cause of the disease and must be used throughout life, which further increases resistance and the economic burden on patients.[3]

Therefore, there is an unmet need for a sensitive tool, preferably an AI-based system, for diagnosing, managing, and monitoring autoimmune disease, as shown in **Figure 1**. Artificial intelligence (AI) is the concept indicating the use of computational systems to execute tasks which normally involve the use of human intelligence. Machine learning (ML), an element of AI, enables systems to learn patterns from data without being programmed directly, and deep learning (DL), another component of ML, employs multilayered neural networks to recognize complex patterns. AI, as a computational process, can perform complex analyses using multivariate data and rapidly predict disease or treatment outcomes. In recent times, there have been significant shifts in the use of AI in healthcare, primarily ML, which indeed support decision-making using multimodal datasets such as genomics, proteomics, metabolomics, imaging, and electronic health records (EHRs), along with complex neural networks.[4] In brief, AI/ML can play a decisive role in risk stratification, early detection, and prognostication, and, accordingly, suggest personalized.[4] The present review aimed to provide a timely update on the role of AI/ML in autoimmune disease, discussing current updates in the context of RA, SLE, MS, T1DM, and IBD. Additionally, we have discussed the role of ML in

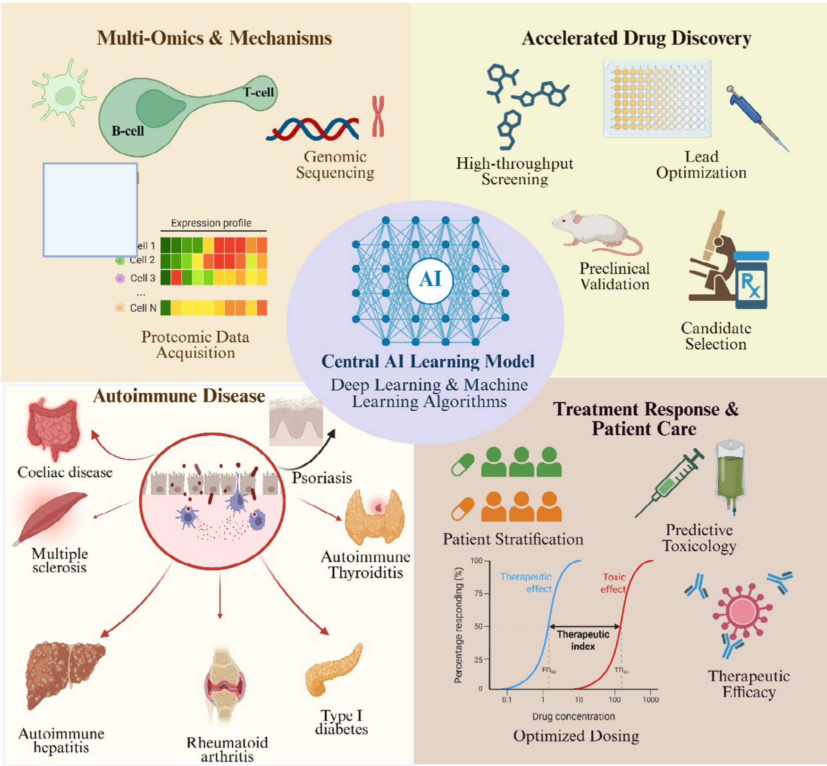


Fig 1 | Showing the emerging role of AI/ML in the diagnosis, management, monitoring, personalized care, and drug discovery for autoimmune disease

Data availability statement: This is a review paper, and we have already submitted the data in paper itself. But if data is required during peer review process, we will make it avaialble.

personalized medicine for autoimmune diseases, current or emerging challenges, and outlook.

Review Methodology

Scope and Design

This article is a narrative review that summarizes and critically appraises published applications of AI, ML, and DL in major autoimmune diseases (SLE, RA, IBD, MS, and T1DM). The review focuses on clinically relevant tasks (diagnosis, risk stratification, flare prediction, treatment response, and monitoring) and highlights translational requirements for safe deployment.

Data Sources and Search Strategy

We searched PubMed/MEDLINE, Scopus, and Google Scholar from database inception to December 31, 2025 (final search date: December 31, 2025). The PubMed search string was: ("autoimmune" OR "autoimmune disease" OR "rheumatoid arthritis" OR "systemic lupus erythematosus" OR "multiple sclerosis" OR "inflammatory bowel disease" OR "ulcerative colitis" OR "Crohn" OR "type 1 diabetes") AND ("machine learning" OR "deep learning" OR "artificial intelligence" OR "neural network" OR "support vector machine" OR "random forest" OR "gradient boosting" OR "XGBoost" OR "natural language processing"). Equivalent adaptations were used for Scopus and Google Scholar. Reference lists of included papers and relevant reviews were hand-searched for additional eligible studies.

Eligibility Criteria

We included peer-reviewed original studies that developed, validated, or evaluated AI/ML/DL models using human data in autoimmune diseases and reported measurable model performance (e.g., AUC, sensitivity/specificity, accuracy, F1, or calibration metrics). We excluded editorials, commentaries, purely theoretical/simulation studies without human data, and abstracts without sufficient methodological details.

Study Selection and Data Extraction

Two reviewers independently screened titles/abstracts and then full texts; disagreements were resolved by discussion. We extracted: disease indication, clinical task, data modality (imaging, EHR/NLP, omics, wearable/proxies, multimodal), cohort size and setting (single vs multicenter), model family, feature engineering, validation approach (internal split or cross-validation, external validation, prospective testing), key discrimination metrics, and whether calibration and explainability were reported.

Quality Appraisal and Risk of Bias

To strengthen methodological transparency, each included predictive model study was appraised using a structured tool suitable for clinical prediction models (e.g., PROBAST for risk of bias and applicability), with additional ML-specific checks (data leakage prevention, proper separation of training/validation/test sets, handling of class imbalance, and reporting of hyperparameter tuning). We summarize common risks (single-center development, limited external validation, and overreliance on accuracy) and their impact on clinical readiness.

Evidence Synthesis

Given heterogeneity in diseases, endpoints, and validation strategies, we performed a qualitative synthesis. We organized evidence by disease and clinical task and provided standardized comparative tables of modalities, model types, validation, and performance. Where claims of very high performance are reported, we explicitly note whether external validation, calibration, and prospective evaluation were performed.

Reporting Framework

Tables 1–3 present study characteristics, model/validation features, and performance/readiness indicators across diseases.

Fundamentals of ML in Autoimmune Disease: In the field of autoimmune disease, AI/ML has contributed significantly to diagnosis and management. Considering ML, it is a subset of AI and primarily learns and improves itself from data rather than programming. In the autoimmune disease, ML supports diagnosis, biomarker selection, and correlation with EHRs, imaging repositories, and multi-omic records.[3] ML can thus distinguish between SLE and RA more accurately than the traditional approach and analyze the image to predict the probability of bone involvement in RA in advance. ML is classified as supervised, unsupervised, semi-supervised, and reinforcement learning, as shown in **Figure 2.** In supervised learning, models are trained on a particular set of data/samples, where each sample has a known outcome.[5] In other words, this model trains from input to output, producing an output for new or unseen data. In autoimmune disease, this model is used for disease classification and risk prediction. Also, for predicting diagnoses based on genetic or laboratory data, classifiers, primarily support vector machines (SVMs), gradient boosting machines, or random forests (RFs), are commonly used.[5]

In unsupervised learning, the algorithm is designed to precisely identify patterns or produce outputs without predefined training or label datasets. This model can be used to identify molecular subgroups using previously unexplored genetic data.[6] This model is primarily used for exploratory analysis and the identification of novel biomarkers and is not commonly used to predict disease outcomes or inform treatment decisions.[6] Reinforcement learning primarily learns from environmental factors. In other words, this model, upon action, is either rewarded or penalized and, over time, is trained, leading to the production of the best or most precise outcome.[5,6] In autoimmune disease, its use is nascent, but over time, it may be better optimized and contribute to the field.

Recently, there has been growing interest in hybrid approaches that combine DL with ensemble methods and structured clinical variables. Deep neural networks such as convolutional neural networks (CNNs) remain central for imaging-heavy tasks (radiology, histology, MRI, endoscopy), while tree-based ensembles (e.g., gradient boosting, XGBoost) and RFs are often competitive for tabular clinical, laboratory, and multi-omic data. Natural language processing can be applied to EHR narratives to extract phenotypes, flares, and treatment response signals. The choice of model should be driven by data modality, sample size, interpretability requirements, and validation strategy rather than by a single "best" algorithm.

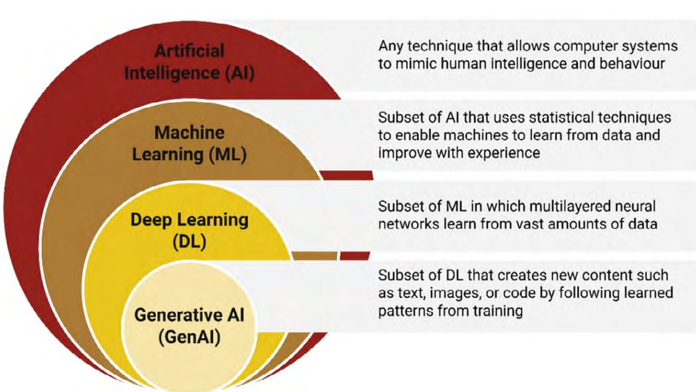


Fig 2 | Showing the classification of artificial intelligence

Role of ML in Autoimmune Disease

Systemic Lupus Erythematosus

SLE is a systemic autoimmune disease where healthy cells are attacked by the hyperactivated immune system, and the prevalence of SLE is 1.5–11 in 100,000 patients per year, with higher prevalence in Black, Asian, and women. ML has been used in the diagnosis and management of therapy. In a systematic review and meta-analysis, Zhou et al.[9] used ML, and the sensitivity and specificity were 0.90 and 0.89, respectively. Li et al.[10] used the 2021 ML (multimodal-based algorithm) and analyzed six proteins to diagnose SLE. Adamichou et al.[11] used RFs on 802 subjects with SLE and rheumatological disease. The outcome showed an accuracy of 94% and a sensitivity of 93.8% against the SLE risk probability index. The LASSO-LR model was used by Han et al.[12] to predict progression from SLE to SLE-SS. A SVM model was used by Tan et al.[13] to diagnose NPSLE, and the results showed accuracy, sensitivities, and specificities of 94.9%, 91.3%, and near-100% (single dataset; requires external validation), respectively. Choi et al.[14] used the longitudinal clustering technique on 805 patients, and the findings showed that SLE patients have a 10% higher risk of CVD. Hence, ML could be a promising tool for early SLE detection, risk prediction, and treatment decisions.

Rheumatoid Arthritis

Rheumatoid arthritis is one of the common systemic arthritides typically associated with chronic inflammation, leading to extraarticular organs and joints. Despite advances in the diagnosis and management of RA, there is still a need for greater specificity and accuracy. A CNN model was developed by Ahalya et al.[15] for RA identification using X-ray images, with sensitivities and specificities of 95% and 94%, respectively. Lim et al. (2023) used ML to detect single-nucleotide polymorphisms in the training data of RA patients, and in another study, Guo et al.[16] used an ML algorithm, network analysis, and RFs to explore biomarkers for RA from the GEO database. The results identified POLE4, AKR1C3, and MCEE as potential biomarkers. Mehta et al.[17] used a RF algorithm to differentiate osteoarthritis from RA using H&E-stained synovial tissue sections. The outcome showed 82% accuracy (micro-AUC 0.87 ± 0.04). In one study, 240 thermal images of the hands of RA and healthy individuals were used, and k-means clustering was employed for hot spot segmentation. Among three classifier models, the LogitBoost classifier showed the best accuracy (93.75%), followed by the quantum SVM (92.7%).[18] Gossec et al. reported flares in patients with RA and axial spondyloarthritis in the ActConnect study, with average sensitivities and specificities of 96% and 97%, respectively.

Inflammatory Bowel Diseases

IBD is among the most common gastrointestinal autoimmune diseases, characterized by inflammation, and affects more than 7 million patients worldwide. Diagnosis and management of IBD are critical, as they involve an integrated approach that includes imaging, laboratory findings, and histological analysis. Additionally, its management is challenging due to its complex etiology. A study by Takenaka et al.[21] using CNNs to assess endoscopic and histological images reported 90% and 93% accuracy for histological and endoscopic data, respectively. Quénéhervé et al.[22] used AI-based laser endomicroscopy for mucosal healing, and sensitivity and specificity were near-100% (single dataset; requires external validation). When natural language processing (NLP) was used in EHRs to predict disease flare and treatment response, the results were promising. However, AI/ML has not yet been thoroughly studied in IBD, but evidence to date suggests immense potential for diagnosis, differential diagnosis, and management.

Type 1 Diabetes Mellitus (T1DM)

T1DM is an autoimmune disease that causes β-cell destruction and significantly affects patients' quality of life. In recent times, ML has been used for diagnosis, management, and monitoring of disease using genetic, metabolic, or immunological data. Cheheltani et al.[23] used ML to differentiate T2TD and T1DM. Oviedo et al.[24] used ML to predict hypoglycemia, and the outcome showed a 37% reduction in hypoglycemia. Cederblad et al.[25] used ML to confirm the causes of hypoglycemia, and the findings showed a profound role of basal insulin pressure and bolus, at 44% and 27%, respectively. Indeed, ML has demonstrated a promising impact in the diagnosis and management of T1DM. However, the lack of prospective validation limits its widespread application. In the future, integrating genomics, proteomics, metabolomics, and EHR may improve early diagnosis and management of T1DM.

Multiple Sclerosis

MS is a chronic autoimmune disease of the CNS and is primarily characterized by neurodegeneration and demyelination. The clinical manifestation of autoimmune disease causes disabilities and considerable socioeconomic pressure. MRI is primarily used for diagnosis, and accurate diagnoses are often missed. AI/ML plays a critical role in the diagnosis, management, and monitoring of MS. ML models, such as SVM, RF, and neural nets, are used, along with brain MRI data, to diagnose or score the disease (EDSS score).[26] In one published study, the use of ML for diagnosing MS achieved a sensitivity and specificity of 60%–80%.[27] Moreover, when imaging data, laboratory reports, genomics, and MRI details, such as lesion location or volume, are integrated with ML, accuracy is significantly improved.

Other Autoimmune Disease

Apart from the above-discussed autoimmune disease and the role of ML, there are other autoimmune diseases, where the role of ML is critical. Graves' disease and Hashimoto's thyroiditis are among such diseases. In one study, ML was used to differentiate Graves' ophthalmopathy from healthy individuals. SVM, k-nearest neighbor, and generalized regression neural network were used in the analysis, and sensitivity and specificity of more than 90% were achieved. In another study, ML was used to predict prognosis and identify responders to first-line glucocorticoid therapy among patients with Graves' ophthalmopathy. The result of an AI application project might personalize treatment options for patients with moderate-to-severe, active Graves' ophthalmopathy. For the differential diagnosis of thyrotoxicosis, ML algorithms were used in combination with EHR data, yielding more reliable reports of RF. Celiac disease is another autoimmune disease that primarily affects the small intestine and is caused by sensitivity to gluten in the diet. The prevalence is 1 in 100, and approximately 22% of first-degree relatives have an increased risk. Notably, undiagnosed cases may range from 80% to more than 80%. In one of the early studies, capsule endoscopy was used to train a deep-CNN (GoogLeNet) and to evaluate pathological involvement. The finding showed near-100% (single dataset; requires external validation) accuracy in diagnosing celiac disease. To correlate pathology and genetic expression in primary biliary cholangitis, a cDNA microarray was used.

Table 1 | Studies Applying ML in Autoimmune Diseases (Classification and Screening)

Disease	Study (Year)	Journal	ML Used	Clinical Task	Data Type	Study Type	Notes
SLE	Zhou et al. (2022)	Comput Intell Neurosci	Yes	Diagnosis (meta-analysis)	Multi-study	Systematic review/ meta-analysis	Not an original ML model
SLE	Li et al. (2022)	Front Immunol	Possibly	Biomarker discovery	Proteomics + scRNA-seq	Original research	ML usage is not explicit
SLE	Adamichou et al. (2021)	Ann Rheum Dis	Yes	Diagnosis support	Clinical + serology	Original ML model	SLERPI model
SLE	Han et al. (2023)	J Clin Med	Yes	Prognosis (SLE–SS overlap)	Clinical	Original ML model	LASSO-LR
SLE	Tan et al. (2022)	Math Biosci Eng	Yes	NPSLE diagnosis	Clinical + neuro	Original ML model	SVM
SLE	Choi et al. (2023)	Ann Rheum Dis	Yes	Risk stratification	Longitudinal autoantibodies	Original ML study	Clustering
RA	Ahalya et al. (2022)	Proc Inst Mech Eng H	Yes	Diagnosis/ classification	X-ray imaging	Original research	CNN on hand radiographs
RA	Mehta et al. (2023)	Arthritis Res Ther	Yes	Differential diagnosis (RA vs OA)	Histology (H&E synovium)	Original research	Random forest; micro-AUC reported

DOI: https://doi.org/10.70389/PJI.100009 | Premier Journal of Immunology 2026;5:100009

RA	Gossec et al. (2019)	Arthritis Care Res	Yes	Flare detection	Wearables (activity)	Original research	ML on activity tracker features
IBD	Takenaka et al. (2020)	Gastroenterology	Yes	Endoscopic severity/ evaluation	Endoscopic images	Original research	Deep neural network; validated dataset
IBD	Quénéhervé et al. (2019)	Gastrointest Endosc	Yes	Mucosal architecture / healing assessment	Confocal laser endomicroscopy	Original research	Computer-based quantitative analysis
T1DM	Cheheltani et al. (2022)	Diabetes Res Clin Pract	Yes	Misdiagnosis prediction	EHR/labs	Original research	Adult-onset T1DM prediction
T1DM	Oviedo et al. (2019)	Comput Methods Programs Biomed	Yes	Hypoglycemia prediction	Glucose self-monitoring + insulin info	Original research	ML to reduce postprandial hypoglycemia
MS	Yousef et al. (2024)	J Neurol	Review	Progression/ outcomes prediction	MRI biomarkers	Narrative review	Summarises ML/ MRI biomarkers and pitfalls

Table 2 | Model Characteristics, Input Modalities, and Validation Strategies of Included Studies

Disease	Study (Year)	Input Modality	ML Model Type	Feature Engineering	Internal Validation	External Validation	Prospective Testing	Notes
SLE	Adamichou et al. (2021)	Clinical + serology	Random Forest	Manual + automated	Yes	No	No	SLERPI diagnostic tool
SLE	Han et al. (2023)	Clinical variables	LASSO + Logistic Regression	Manual	Yes	No	No	Overlap prediction
SLE	Tan et al. (2022)	Clinical + neuro data	Support Vector Machine	Manual	Yes	No	No	NPSLE diagnosis
SLE	Choi et al. (2023)	Longitudinal autoantibodies	Clustering ML	Automated	Yes	No	No	Risk stratification
RA	Ahalya et al. (2022)	X-ray imaging	CNN (DL)	Automated feature learning	Yes	No	No	Single/ limited center imaging data
RA	Mehta et al. (2023)	Histology (H&E)	Random Forest	Patch-based + engineered features	Yes	No	No	RA vs OA discrimination
IBD	Takenaka et al. (2020)	Endoscopic images	Deep neural network	Automated	Yes	External (reported)	No	Ulcerative colitis endoscopy evaluation
T1DM	Cheheltani et al. (2022)	EHR/lab data	Supervised ML	Manual/ engineered	Yes	Not clear	No	Predicting misdiagnosed T1DM

A summary of the reported predictive performance, explainability, and readiness of the included ML models to the real world is presented in Table 3. Most of the models are in an experimental or pilot phase, although internal performance measures are high because of the lack of external validation, calibration studies, and future clinical testing.

Table 3 | Model Performance, Explainability, and Clinical Readiness of Included ML Studies

Disease	Study (Year)	Task	Accuracy/AUC	Sensitivity	Specificity	Calibration Reported	Explainability Used	Clinical Readiness Level	Notes
SLE	Adamichou et al. (2021)	Diagnosis support	Accuracy ≈ 94%	93.8%	Not reported	No	No	Experimental	Internal validation only
SLE	Han et al. (2023)	Overlap prediction	AUC not clearly reported	Not reported	Not reported	No	No	Experimental	Needs external validation
SLE	Tan et al. (2022)	NPSLE diagnosis	Accuracy ≈ 94.9%	91.3%	100%	No	No	Experimental	Single-center

Disease	Study (Year)	Task	Accuracy/AUC	Sensitivity	Specificity	Calibration Reported	Explainability Used	Clinical Readiness Level	Notes
SLE	Choi et al. (2023)	Risk stratification	Not reported	Not reported	Not reported	No	No	Experimental	Cluster-based
RA	Ahalya et al. (2022)	RA identification	Reported high performance	Reported	Reported	No	Saliency not described	Experimental	Imaging model; needs external validation
RA	Mehta et al. (2023)	RA vs OA discrimination	micro-AUC ~0.87	–	–	No	Not detailed	Experimental	Histology-based; limited generalizability
IBD	Takenaka et al. (2020)	Endoscopic evaluation (UC)	High accuracy/ AUROC reported	–	–	Not clearly reported	Not detailed	Translational research	External validation reported; calibration unclear

Table 4 | Common Methodological Limitations and Translational Gaps Across Included Studies

Domain	Observed Limitation	Description	Impact on Clinical Translation	Examples from Included Studies
Dataset size	Small sample sizes	Most studies were trained on small or moderate cohorts	High risk of overfitting, unstable performance	SLE, RA imaging, celiac CNN studies
Data source	Single-center datasets	The majority of studies used data from a single institution	Poor generalizability across populations	Most SLE, RA, and IBD studies
Population diversity	Limited demographic diversity	Few studies reported race, ethnicity, or socioeconomic stratification	Risk of bias and health inequity	SLE and MS studies
Validation	Lack of external validation	Models were rarely tested on independent datasets	Inflated performance estimates	Nearly all included studies
Validation	No prospective testing	None of the studies were prospectively evaluated	Unknown real-world utility	All disease groups
Outcome definition	Heterogeneous endpoints	Different definitions of diagnosis, flare, and remission	Limits cross-study comparability	IBD, RA flare models
Feature engineering	Poor transparency	Feature selection steps are often underreported	Low reproducibility	Multiple ML studies
Model reporting	Incomplete hyperparameter reporting	Many studies did not report tuning methods	Reproducibility issues	Imaging CNN models
Evaluation metrics	Overreliance on accuracy	Limited use of calibration, decision-curve analysis	Misleading clinical utility	Most disease models
Calibration	Not reported	No studies assessed probability calibration	Unsafe for decision support	All models
Explainability	Absent or minimal	Few used SHAP, LIME, and saliency maps	Low clinician trust	Most DL models
Data leakage	Risk of contamination	Improper train–test separation	Artificially high performance	Some imaging studies
Domain shift	No robustness testing	Models not tested on out-of-distribution data	Fragile deployment	All models
Benchmarking	No head-to-head model comparison	Few studies compared multiple algorithms rigorously	Suboptimal model choice	Many RA, SLE studies
Clinical integration	No workflow integration	Models tested in isolation	No deployment readiness	All disease groups
Regulatory framing	Not discussed	No FDA/EMA or device classification	Unknown approval pathway	All studies
Ethical analysis	Superficial	Bias, consent, and privacy are not deeply explored	Legal and trust barriers	Most papers

DOI: https://doi.org/10.70389/PJI.100009 | Premier Journal of Immunology 2026;5:100009

ML-Based Personalized Treatment and Drug Discovery in Autoimmune Disease

The complexity and variation in autoimmune disease have led to the emergence of personalized therapy, as shown in **Figure 3**, in which genetic and environmental factors are considered (Table 4). In contrast, in traditional treatment, they are not taken into account and are based on a one-size-fits-all approach. There is a profound role for AI/ML in the personalized treatment of autoimmune disease, where multiple data are integrated to determine the course of treatment, predict response, and overall improve outcomes.[33] ML or DL can stratify patients suitable for various biological therapies based on multiple omics data and also support the selection of the ideal dose for each patient. Moreover, AI algorithms can play a vital role in treatment decisions by integrating pharmacokinetic or dynamic data with individual factors such as body weight, BMI, EHRs, remote or wearable technology.[33] Moreover, AI-based personalized treatment can also promptly modify the course of treatment based on the response or adverse events.[34] However, ethical considerations related to privacy protection, algorithmic bias, and other factors must be taken into account to ensure an efficient framework and better clinical outcomes.[35]

Apart from the role of AI/ML in personal treatment of autoimmune disease, there is also an emerging role of ML in drug discovery. Deep generative models can effectively predict or propose molecular structures that modulate the immune system.[36] Also, ML or DL can add value to drug repurposing by integrating genetic, clinical trial, and EHR data.[37] Apart from the above-discussed role, ML/DL is also used in the in silico stimulation for drug discovery, for the prediction of drug metabolism, and multi-omic discovery of biomarkers.[36,37]

Challenges, Limitations, and Ethical Considerations

The integration of AI/ML in the diagnosis, management, or monitoring of autoimmune diseases has significantly revolutionized this area. However, certain limitations and ethical considerations also exist. AI/ML primarily integrates complex data from radiological findings, laboratory reports, genomics, and immunology, and therefore needs to be accurate and reliable to support clinical decision-making.[35] Also, in the healthcare system, the diagnostic or treatment protocols differ significantly, and hence, the universal adoption of AI-based decision-making automation remains challenging. Also, as of now, AI/ML is used primarily for research, and translating findings from labs to clinics is another challenge. Sometimes, patient clinical presentations are unique or rare, and supervised/unsupervised/reinforcement-based models may fail or produce false-positive or false-negative results.[35] Also, ethical concerns arise from the integration of ML into the healthcare sector regarding personal information and patients' privacy, including their genetic data and medical records, and hence, data security is an essential component.

Autonomy and trust must not be overlooked, as AI-based recommendations may compromise patients' or physicians' autonomy.[38] AI/ML must complement human-like decision makers rather than replace physicians. Additionally, physicians should have experience with an AI model and its functioning to gel with the technology. Moreover, there is a need for strong, robust regulatory guidelines for the safe and effective use of AI/ML in healthcare.[38]

Future Prospects of ML in Autoimmune Disease

With the advancement in AI-based systems, ML is becoming the forefront in the clinical diagnosis and management of autoimmune disease. These developments result from the integration of multiomic data, the use of ML for early disease diagnosis, and the management of treatment courses.[26] The future prospects of AI in autoimmune disease include better sensitivity, specificity, and generalizability for patients, leading to better clinical outcomes. Moreover, federated learning, an advanced ML technique, can learn from a vast database and support diagnosis and treatment while maintaining data privacy. The future of ML in autoimmune disease can also be seen in terms of early disease diagnosis using wearable technologies and EHRs, and in integrating patients' reported outcomes (PRO) with DL-based models, as shown in **Figure 4**.[36] Notably, the future of AI is also transforming clinical trials, where ML/DL-based algorithms are used for patient selection, randomization, monitoring, and outcome assessment, enabling faster processing than the traditional approach.[33]

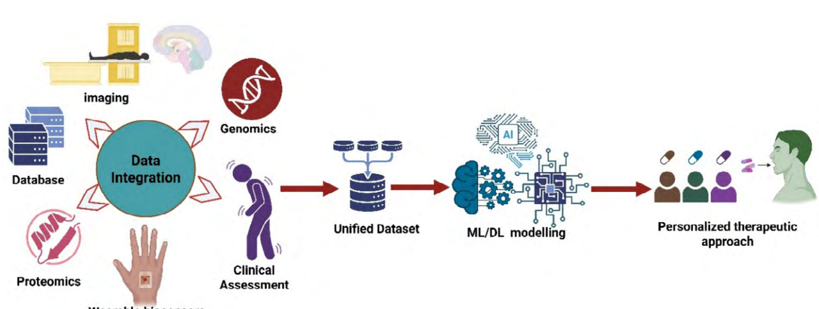


Fig 3 | Showing the role of AI/ML in personalized treatment in autoimmune disease

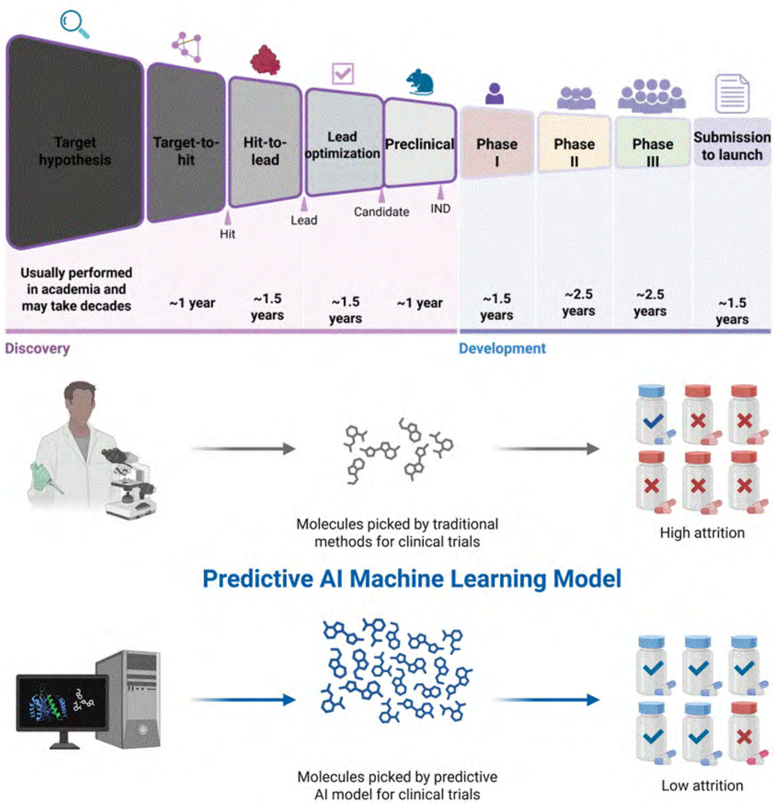


Fig 4 | Showing the emerging role of AI and ML in clinical trials

Conclusion

With continuous upgrades and improvements, AI is becoming an integrated or valued partner in the healthcare sector, where significant advances in diagnosis, management, and treatment have been made in autoimmune disease. The use of CNNs in radiological images, the discovery of biomarkers, the use of predictive models for early disease detection, the use of advanced DL with multiomic data, and the use of EHRs or PROs to optimize treatment are continuously improving patients' quality of life. However, with these advancements, issues such as data privacy protection and the handling of trust-related dilemmas between patients and AI/ML need to be addressed. To achieve this, a collaborative approach between a clinician, an immunologist, and a data scientist is needed that will eventually transform the paradigm of autoimmune disease diagnosis, management, and treatment.

Conflict of Interest: The authors declare that there are no conflicts of interest associated with this study

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

Acknowledgment: The authors would also like to acknowledge the contribution of all researchers whose works were used in this review. We also recognize the useful comments from peer reviewers, which helped us enhance the quality and clarity of this manuscript.

Disclaimer: This article represents the views and opinions of the authors and may not be representative of the policies or views of any of the related bodies. The manuscript is purely academic and research-based and is not meant to be medical or clinical guidance.

References

1 Zeng SQ, Zhen JH, Pu Y, et al. Global, regional, and national burden of autoimmune disease in older adults (≥60 years) from 1990 to 2021: Results from the Global Burden of Disease Study 2021. J Nutr Health Aging. 2025;29:100681. https://doi.org/10.1016/J.JNHA.2025.100681

2 Danieli MG, Brunetto S, Gammeri L, et al. Machine learning application in autoimmune diseases: State of art and future prospectives. Autoimmun Rev. 2024;23:103496. https://doi.org/10.1016/J.AUTREV.2023.103496

3 Mane DV, Deshmukh AN, Ambare RH, et al. AI in autoimmune diseases: Transforming diagnosis and treatment. J Pharm Biol Sci. 2025;12:109–18. https://doi.org/10.18231/J.JPBS.2024.017

4 Cao C, Zhao W, Guo J, et al. Leveraging artificial intelligence and machine learning for unraveling pathogenesis and advancing precision medicine in autoimmune diseases. Innov Med. 2025;3:100154–1. https://doi.org/10.59717/J.XINN-MED.2025.100154

5 Uc Castillo JL, Marín Celestino AE, Martínez Cruz DA, et al. A systematic review of machine learning and deep learning approaches in Mexico: Challenges and opportunities. Front Artif Intell. 2024;7:1479855. https://doi.org/10.3389/FRAI.2024.1479855/PDF

6 Razzaq K, Shah M. Machine learning and deep learning paradigms: From techniques to practical applications and research frontiers. Computers. 2025;14:93. https://doi.org/10.3390/COMPUTERS14030093.

7 Tariq R, Afzali A. Artificial intelligence in inflammatory bowel disease: Innovations in diagnosis, monitoring, and personalized care. Therap Adv Gastroenterol. 2025;18:17562848251357408. https://doi.org/10.1177/17562848251357407

8 Kegerreis B, Catalina MD, Bachali P, et al. Machine learning approaches to predict lupus disease activity from gene expression data. Sci Rep. 2019;9:9617–. https://doi.org/10.1038/s41598-019-45989-0

9 Zhou Y, Wang M, Zhao S, et al. Machine learning for diagnosis of systemic lupus erythematosus: A systematic review and meta-analysis. Comput Intell Neurosci. 2022;2022:1–14. https://doi.org/10.1155/2022/7167066

10 Li Y, Ma C, Liao S, et al. Combined proteomics and single cell RNA-sequencing analysis to identify biomarkers of disease diagnosis and disease exacerbation for systemic lupus erythematosus. Front Immunol. 2022;13:969509. https://doi.org/10.3389/FIMMU.2022.969509/BIBTEX

11 Adamichou C, Genitsaridi I, Nikolopoulos D, et al. Lupus or not? SLE Risk Probability Index (SLERPI): A simple, clinician-friendly machine learning-based model to assist the diagnosis of systemic lupus erythematosus. Ann Rheum Dis. 2021;80:758–66. https://doi.org/10.1136/annrheumdis-2020-219069

12 Han Y, Jin Z, Ma L, et al. Development of clinical decision models for the prediction of systemic lupus erythematosus and Sjogren's syndrome overlap. J Clin Med. 2023;12:535. https://doi.org/10.3390/JCM12020535/S1

13 Tan G, Huang B, Cui Z, et al. A noise-immune reinforcement learning method for early diagnosis of neuropsychiatric systemic lupus erythematosus. Math Biosci Eng. 2022;19:2219–39. https://doi.org/10.3934/MBE.2022104

14 Choi MY, Chen I, Clarke AE, et al. Machine learning identifies clusters of longitudinal autoantibody profiles predictive of systemic lupus erythematosus disease outcomes. Ann Rheum Dis. 2023;82:927–36. https://doi.org/10.1136/ard-2022-223808

15 Ahalya RK, Umapathy S, Krishnan PT, et al. Automated evaluation of rheumatoid arthritis from hand radiographs using machine learning and deep learning techniques. Proc Inst Mech Eng H. 2022;236:1238–49. https://doi.org/10.1177/09544119221109735

16 Guo Z, Ma Y, Wang Y, et al. Identification and validation of metabolism-related genes signature and immune infiltration landscape of rheumatoid arthritis based on machine learning. Aging. 2023;15:3807–25. https://doi.org/10.18632/AGING.204714

17 Mehta B, Goodman S, DiCarlo E, et al. Machine learning identification of thresholds to discriminate osteoarthritis and rheumatoid arthritis synovial inflammation. Arthrit Res Ther. 2023;25:31–. https://doi.org/10.1186/S13075-023-03008-8.
18 Ahalya RK, Snekhalatha U, Dhanraj V. Automated segmentation and classification of hand thermal images in rheumatoid arthritis using machine learning algorithms: A comparison with quantum machine learning technique. J Therm Biol. 2023;111:103404. https://doi.org/10.1016/J.JTHERBIO.2022.103404
19 Gossec L, Guyard F, Leroy D, et al. Detection of flares by decrease in physical activity, collected using wearable activity trackers in rheumatoid arthritis or axial spondyloarthritis: An application of machine learning analyses in rheumatology. Arthritis Care Res (Hoboken). 2019;71:1336–43. https://doi.org/10.1002/ACR.23768
20 Alatab S, Sepanlou SG, Ikuta K, et al. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2020;5:17–30. https://doi.org/10.1016/S2468-1253(19)30333-4
21 Takenaka K, Ohtsuka K, Fujii T, et al. Development and validation of a deep neural network for accurate evaluation of endoscopic images from patients with ulcerative colitis. Gastroenterology. 2020;158:2150–7. https://doi.org/10.1053/j.gastro.2020.02.012
22 Quénéhervé L, David G, Bourreille A, et al. Quantitative assessment of mucosal architecture using computer-based analysis of confocal laser endomicroscopy in inflammatory bowel diseases. Gastrointest Endosc. 2019;89:626–36. https://doi.org/10.1016/j.gie.2018.08.006
23 Cheheltani R, King N, Lee S, et al. Predicting misdiagnosed adult-onset type 1 diabetes using machine learning. Diabetes Res Clin Pract. 2022;191:110029. https://doi.org/10.1016/j.diabres.2022.110029
24 Oviedo S, Contreras I, Bertachi A, et al. Minimizing postprandial hypoglycemia in type 1 diabetes patients using multiple insulin injections and capillary blood glucose self-monitoring with machine learning techniques. Comput Methods Programs Biomed. 2019;178:175–80. https://doi.org/10.1016/J.CMPB.2019.06.025
25 Cederblad L, Eklund G, Vedal A, et al. Classification of hypoglycemic events in type 1 diabetes using machine learning algorithms. Diabetes Therapy. 2023;14:953–65. https://doi.org/10.1007/S13300-023-01403-7
26 Yousef H, Malagurski Tortei B, Castiglione F. Predicting multiple sclerosis disease progression and outcomes with machine learning and MRI-based biomarkers: A review. J Neurol. 2024;271:6543–72. https://doi.org/10.1007/S00415-024-12651-3
27 Pilehvari S, Morgan Y, Peng W. An analytical review on the use of artificial intelligence and machine learning in diagnosis, prediction, and risk factor analysis of multiple sclerosis. Mult Scler Relat Disord. 2024;89:105761. https://doi.org/10.1016/J.MSARD.2024.105761
28 Li J, Chen F, Huang G, et al. Identification of Graves' ophthalmology by laser-induced breakdown spectroscopy combined with machine learning method. Front Optoelectr. 2020;14:321–8. https://doi.org/10.1007/S12200-020-0978-2
29 Wang Y, Wang H, Li L, et al. Novel observational study protocol to develop a prediction model that identifies patients with Graves' ophthalmopathy insensitive to intravenous glucocorticoids pulse therapy. BMJ Open. 2021;11:e053173. https://doi.org/10.1136/BMJOPEN-2021-053173
30 Kim J, Baek HS, Ha J, et al. Differential diagnosis of thyrotoxicosis by machine learning models with laboratory findings. Diagnostics. 2022;12:1468. https://doi.org/10.3390/DIAGNOSTICS12061468
31 Zhou T, Han G, Li BN, et al. Quantitative analysis of patients with celiac disease by video capsule endoscopy: A deep learning method. Comput Biol Med. 2017;85:1–6. https://doi.org/10.1016/J.COMPBIOMED.2017.03.031
32 Kim JW, Ye Q, Forgues M, et al. Cancer-associated molecular signature in the tissue samples of patients with cirrhosis. Hepatology. 2004;39:518–27. https://doi.org/10.1002/HEP.20053
33 Afzal M, Sah AK, Agarwal S, et al. Advancements in the treatment of autoimmune diseases: Integrating artificial intelligence for personalized medicine. Trends Immunother. 2024;8:8970. https://doi.org/10.24294/TI8970
34 Carini C, Seyhan AA, Carini claudiocarini C, et al. Tribulations and future opportunities for artificial intelligence in precision medicine. J Transl Med. 2024;22:411–. https://doi.org/10.1186/S12967-024-05067-0
35 Bekbolatova M, Mayer J, Ong CW, et al. Transformative potential of AI in healthcare: Definitions, applications, and navigating the ethical landscape and public perspectives. Healthcare. 2024;12:125. https://doi.org/10.3390/HEALTHCARE12020125
36 Bassey GE, Daniel EA, Okesina KB, et al. Transformative role of artificial intelligence in drug discovery and translational medicine: Innovations, challenges, and future prospects. Drug Des Devel Ther. 2025;19:7493. https://doi.org/10.2147/DDDT.S538269
37 Mahajan A, LaChance AH, Rodman A, et al. Artificial intelligence for autoimmune diseases. Npj Dig Med. 2025;8:628–. https://doi.org/10.1038/s41746-025-02015-0
38 Alanzi T, Alhajri A, Almulhim S, et al. Artificial intelligence and patient autonomy in obesity treatment decisions: An empirical study of the challenges. Cureus. 2023;15. https://doi.org/10.7759/CUREUS.49725