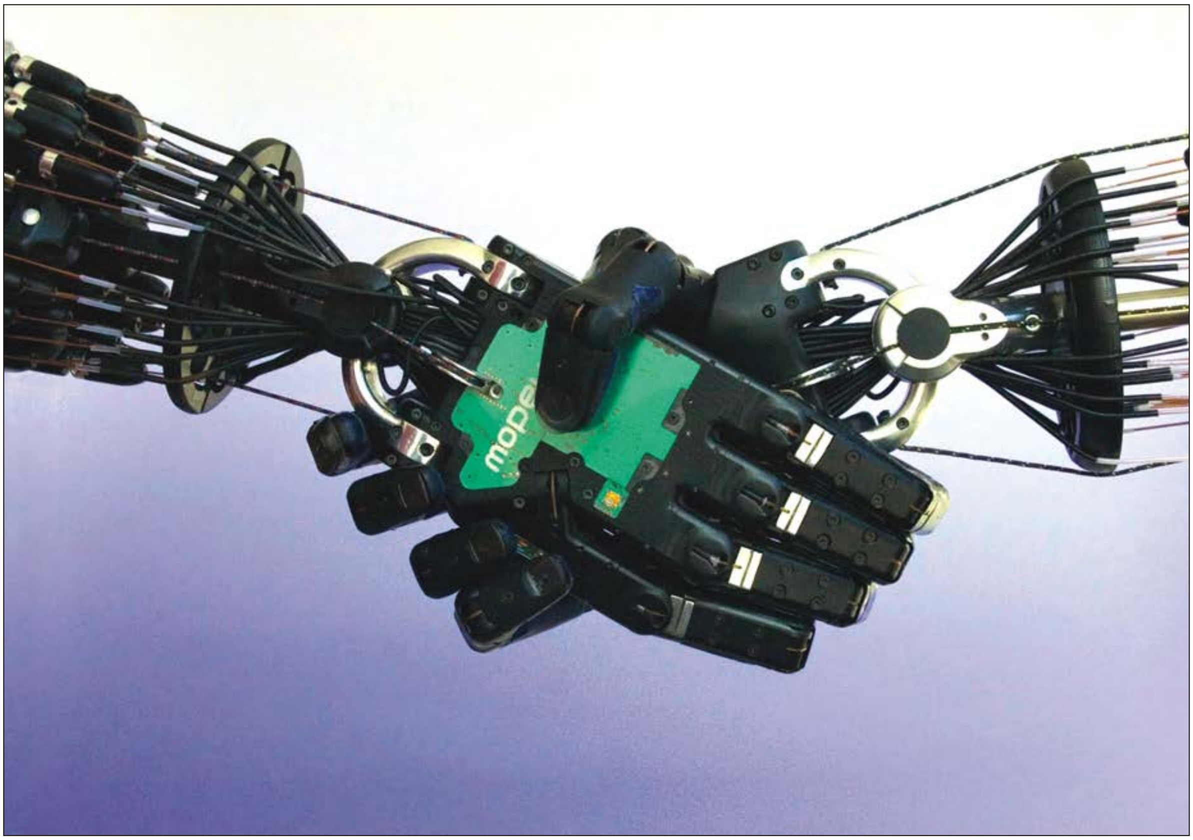

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Review Article

Machine Learning in Haematological Malignancies: From Early Detection to Precision Therapy

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Abstract

Haematological malignancies, including leukaemia, lymphoma and multiple myeloma, constitute a significant global cancer burden and remain the leading causes of cancer-related mortality. While advances in molecular profiling, cytogenetics and immunophenotyping have enhanced disease classification and risk stratification, these approaches are often costly, time-intensive and subject to interpretive variability. Machine Learning (ML), a core domain of artificial intelligence, is emerging as a transformative tool in haematology, offering scalable solutions for diagnosis, prognostication and therapeutic decision-making. This review synthesizes evidence from recent applications of ML in haematological malignancies, focusing on diagnostic imaging models, multi-modal data integration frameworks, prognostic algorithms utilizing multi-omics datasets and predictive platforms for therapy optimization and transplantation outcomes. Convolutional neural networks demonstrate high accuracy in classifying malignant cells from peripheral blood smears and histopathology, reducing inter-observer variability and improving workflow efficiency. Multi-modal systems integrating imaging, genomic and clinical variables enhance diagnostic precision. Prognostic ML models outperform conventional scoring systems in predicting survival, relapse risk and treatment response. Deep learning architectures, including autoencoders, uncover latent biological signatures linked to disease progression and drug resistance. In therapeutics, ML supports dose optimization, toxicity prediction and drug-response forecasting. Predictive tools in hematopoietic stem cell transplantation further improve patient selection and risk stratification. Machine learning is redefining precision oncology in haematological malignancies by improving diagnostic reproducibility, refining prognostic accuracy and enabling individualized therapy. Its continued integration into clinical workflows holds promise for better outcomes and more efficient haematologic cancer care.

Key words: Machine learning, haematological malignancies, early detection, precision therapy, predictive oncology

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Haematological malignancies, including leukaemias, lymphomas and multiple myeloma, account for over 10% of global cancer diagnoses and remain major causes of cancer mortality[1]. Although advances in cytogenetics, molecular profiling and immunophenotyping have improved disease classification and risk stratification, these approaches are often expensive, time-intensive and subject to interpretive variability. Artificial Intelligence (AI), particularly machine learning (ML), has emerged as a transformative tool in oncology due to its capacity to analyze complex datasets and integrate imaging, genomic and clinical information[2].

In early detection, Convolutional Neural Networks (CNNs) automate feature extraction from blood smears, histopathology and bone marrow aspirates, improving diagnostic accuracy and reducing inter-observer variability[3-5]. Multi-modal frameworks combining imaging with genomic and clinical data further enhance risk prediction and precision oncology applications[6], though challenges such as dataset standardization and external validation persist[7].

For prognostication, ML models leveraging multi-omics data outperform traditional stratification systems by capturing complex molecular interactions[8,9]. In therapy optimization, ML supports dose adjustment, toxicity prediction, drug-response forecasting and transplantation risk assessment[10,11].

Machine learning applications in haematological malignancies span detection, prognostication and therapy optimization in an integrated framework (Fig. 1).

Overall, ML is reshaping early detection, prognostication and treatment personalization in haematological malignancies. This review synthesizes current evidence and highlights translational challenges and future directions toward precision therapy.

MATERIALS AND METHODS

This investigation was conducted as a systematic review following known methodological standards, including the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria, tailored for artificial intelligence and biomedical research.

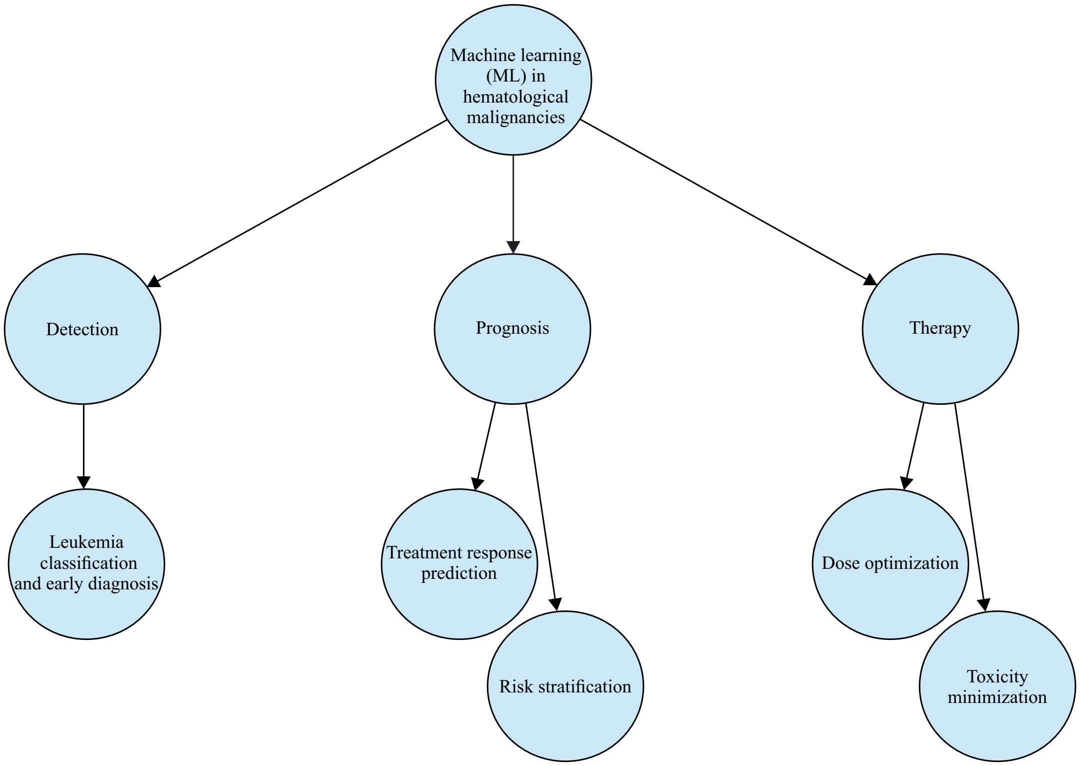

Fig. 1: Tree/Hierarchy schematic of machine learning applications in haematological malignancies

Hierarchical structure highlights the central role of Machine Learning (ML) in three key domains: Detection, prognosis and therapy. Subdomains include leukemia classification and early diagnosis (detection), treatment response prediction and risk stratification (prognosis) and dose optimization and toxicity minimization (therapy)

Identification
Records identified (n = 1380)
↓
Screening
Records after duplicates removed (n = 1020)
Records screened (n = 1020)
Records excluded (n = 780)
↓
Eligibility
Full-text articles assessed (n = 240)
Full-text excluded (n = 204)
↓
Included
Studies included in review (n = 36)

Fig. 2: Prisma flow diagram

This systematic review was conducted in accordance with PRISMA guidelines shown in Fig. 2. A comprehensive literature search was performed across PubMed/MEDLINE, Scopus, Web of Science, IEEE Xplore and Google Scholar covering January 2010 to December 2025. The search was conducted between April, 2025 and February, 2026.

A total of 1,380 records were identified, with 1,020 remaining after duplicate removal. Following title and abstract screening, 240 articles were assessed for full-text eligibility, of which 36 studies met the inclusion criteria and were included in the final synthesis.

The PubMed search strategy included: (“machine learning” OR “artificial intelligence” OR “deep learning”) AND (“haematological malignancies” OR “leukaemia” OR “lymphoma” OR “multiple myeloma”) AND (“diagnosis” OR “prognosis” OR “risk stratification” OR “treatment response” OR “precision medicine”).

Screening was conducted independently by two reviewers using Rayyan software, with disagreements resolved through consensus. Data extraction was performed using a standardized Microsoft Excel template capturing study characteristics, ML models, validation methods and performance metrics.

Data sources and search techniques: The following databases were used for a thorough and repeatable literature search: PubMed/MEDLINE, Scopus, Web of Science Core Collection, IEEE Xplore Digital Library and Google Scholar (for recent articles and grey literature). Studies published between January, 2010 and December, 2025 were included in the search, with a focus on recent developments (2018-2025).

Search terms and query structure: Both free-text and regulated vocabulary were employed. “AND” and “OR”, two Boolean operators, improved the search. “Machine learning”, “artificial intelligence”, “deep learning”, “haematological malignancies”, “blood cancer”, “leukaemia”, “lymphoma”, “multiple myeloma”, “diagnosis”, “classification”, “prognosis”, “risk stratification”, “treatment response”, “precision medicine”, “drug prediction”, “multi-omics”, “genomics” and “clinical decision support” were among the key search terms.

Eligibility criteria

Inclusion criteria:

- Peer-reviewed original research, systematic reviews or meta-analyses
- Studies applying ML/AI methods in haematological malignancies
- Studies addressing diagnosis, prognosis or treatment optimization
- English-language publications
- Studies reporting performance metrics (e.g., accuracy, AUC, sensitivity)

Exclusion criteria:

- Non-AI-based studies
- Studies focused solely on solid tumors
- Editorials, commentaries, conference abstracts without full text
- Duplicate studies
- Studies lacking sufficient methodological detail

Study selection process

Study selection was conducted in two phases:

- Title and abstract screening to remove irrelevant records
- Full-text review for eligibility

A PRISMA flow approach was used to document identification, screening, eligibility and inclusion of studies.

Data extraction: A standardized template was used to systematically extract the following Data: Study characteristics (author, year, country), type of malignancy, dataset type (imaging, genomic, clinical, multi-omics), ML models used (CNN, SVM, Random Forest, deep learning architectures), validation approach (internal/external) and performance metrics (accuracy, AUC, sensitivity, specificity).

Quality assessment and risk of bias: Adapted AI-specific evaluation criteria, such as dataset size and diversity, external validation, model interpretability, risk of overfitting and reproducibility of methods, were used to evaluate the methodological quality of the included studies. Where appropriate, tools like QUADAS-2 (for diagnostic models) and PROBAST (for prediction models) were taken into consideration.

Data synthesis: A quantitative meta-analysis was not carried out because of the variation in study design, datasets and outcome measures. Rather, a structured narrative technique was used to synthesize the findings, which were categorized into: Prognostic modeling, precision therapy and treatment response, early detection and diagnosis, multi-omics integration and decision support systems. ML models and traditional clinical methods were compared.

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) DETECTION: DEEP LEARNING ARCHITECTURES

Early and accurate detection of acute lymphoblastic leukemia (ALL), particularly in pediatric populations, is critical for timely therapy and improved prognosis. Conventional diagnosis based on manual review of peripheral blood smears and bone marrow aspirates is labor-intensive and prone to inter-observer variability. Deep learning (DL) models now enable automated blast detection with accuracy comparable to expert haematologists[3,4].

Hybrid architectures such as MobileNetV2-ResNet18 and MobileNetV2-SVM achieve >95% classification accuracy in differentiating leukemic blasts from normal lymphocytes by combining lightweight feature extraction with deep or machine-learning classifiers. Earlier CNNs (e.g., LeNet, AlexNet) demonstrated feasibility but were limited by overfitting on small datasets[3]. Newer models, including DenseNet and EfficientNet, improve sensitivity through transfer learning and augmentation[12,13].

Figure 3 shows CNN-based hybrid models for automated ALL detection, highlighting improved accuracy, speed and reduced subjectivity.

Benchmark datasets such as C-NMC (ISBI 2019) have enabled robust validation, with ensemble CNN systems exceeding 90-96% accuracy[14]. A DL systems also identifies subtle morphological features such as nuclear texture and chromatin patterns beyond human perception[15]. Lightweight models support deployment in resource-limited settings, while explainable AI tools (e.g., Grad-CAM) enhance interpretability[16].

Despite progress, generalizability remains limited by small, non-standardized datasets, underscoring the need for multi-center validation.

ACUTE MYELOID LEUKEMIA (AML) RISK STRATIFICATION: RANDOM FOREST AND SVM MODELS

Acute Myeloid Leukemia (AML) is a genetically heterogeneous malignancy characterized by recurrent mutations, cytogenetic abnormalities and variable clinical

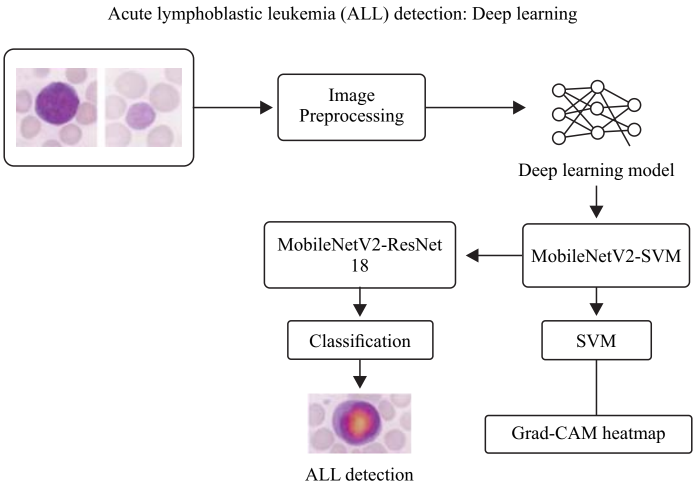
Acute lymphoblastic leukemia (ALL) detection: Deep learning

Fig. 3: CNN-based hybrid deep learning models facilitate automated detection of acute lymphoblastic leukemia (ALL) with >95% accuracy, improving diagnostic speed and reducing observer bias while providing clinically interpretable outputs suitable for low-resource settings.
Acute Lymphoblastic Leukemia, CNN: Convolutional Neural Network and Explainable AI components enhance interpretability and support clinical decision-making

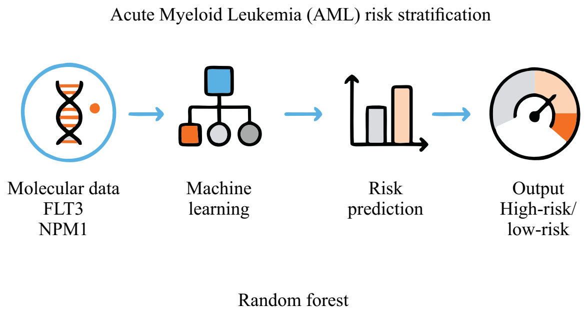

Fig. 4: Random forest and Support Vector Machine (SVM) models integrate genetic and clinical data to generate personalized Acute Myeloid Leukemia (AML) risk predictions, outperforming conventional cytogenetic-based approaches

AML: Acute Myeloid Leukemia, SVM: Support Vector Machine and genetic inputs include mutation and cytogenetic profiles, while clinical variables include hematological and patient history data

outcomes, making accurate risk stratification essential for guiding induction therapy, transplantation decisions and targeted treatment use. Conventional prognostic systems based on cytogenetics and single mutations such as FLT3-ITD and NPM1 provide limited predictive precision due to complex molecular interactions and disease heterogeneity[17,18].

Machine Learning (ML) approaches, particularly Random Forest (RF) and Support Vector Machine (SVM) models, enhance risk prediction by integrating multidimensional clinical and molecular datasets. Li *et al.*[8] showed that combining FLT3 and NPM1 mutations with clinical variables in RF and SVM frameworks significantly improved relapse prediction compared with traditional statistical models. RF algorithms effectively process large genomic datasets while providing feature-importance metrics, whereas SVMs excel in separating high- and low-risk groups within complex data spaces[8].

Figure 4 demonstrates the integration of genomic and clinical data using RF and SVM for personalized AML risk stratification.

Additional studies confirm these advantages. RF and gradient boosting models applied to transcriptomic data improved survival prediction beyond European LeukemiaNet criteria[19], while ensemble ML integrating mutational and clinical variables enhanced prognostic accuracy in older AML cohorts[20]. Multi-omics integration including methylation and gene-expression profiles further refines relapse risk classification[21].

Despite the promise, limitations include retrospective datasets, platform heterogeneity and limited external validation, which constrain clinical translation.

PROGNOSTIC MODELING IN PAEDIATRIC ONCOLOGY

Prognostic modeling in paediatric oncology is increasingly leveraging Machine Learning (ML) to enhance prediction of survival, relapse and treatment-related toxicity. Accurate prognostic tools are particularly critical in children, where balancing curative therapy with long-term quality of life is paramount[22].

Figure 5 illustrates a workflow where clinical and molecular data are processed by ML models to generate personalized prognostic predictions.

Recent systematic reviews highlight that ML models achieve moderate-to-high predictive accuracy in outcomes such as overall survival and event-free survival, especially when integrating variables like age, cytogenetics, MRD status and treatment response[6,22]. These models offer improved stratification compared to conventional statistical approaches, but many lack external validation, limiting their clinical utility.

The ML models have also been applied to toxicity prediction, where they identify children at higher risk for complications such as anthracycline-induced cardiotoxicity, methotrexate-induced hepatotoxicity and bone marrow suppression. Despite promising sensitivity, inconsistent toxicity reporting standards across studies hinder reproducibility and translation into real-world settings[22].

Beyond clinical features, integrative ML approaches now combine genomic and transcriptomic data with conventional clinical predictors, enhancing prognostic accuracy in paediatric leukemias, where genetic heterogeneity is high[8]. However, the majority of these remain proof-of-concept, with large-scale validation pending.

TREATMENT RESPONSE PREDICTION AND THERAPY OPTIMIZATION

In parallel, ML has shown significant utility in predicting treatment response and optimizing therapy schedules in pediatric hematology-oncology. Ramesh *et al.*[23] documented that supervised learning models, including support vector

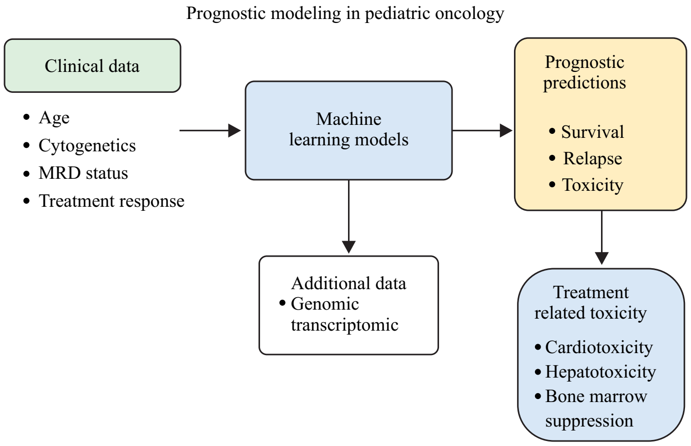

Fig. 5: Machine learning workflow integrating clinical and molecular data for personalized prognostic prediction in pediatric patients

Clinical data include patient demographics and laboratory findings, molecular data include genomic and transcriptomic profiles used for outcome prediction

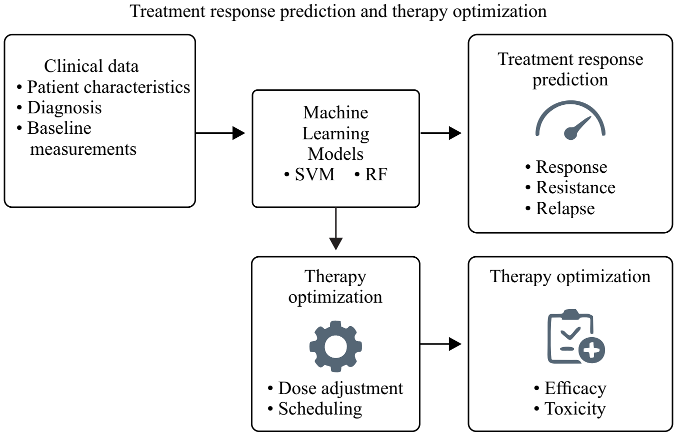

Fig. 6: ML-driven integration of clinical and pharmacogenomic data for personalized therapy and treatment response prediction

Pharmacogenomics refers to genetic influences on drug response, enabling adaptive treatment optimization based on predicted efficacy and safety

machines (SVMs) and random forests (RFs), predicted chemotherapy response in small cohorts, allowing for early therapy escalation or de-escalation.

Therapy optimization is another promising domain, particularly through dose adaptation and scheduling. Reinforcement learning models have simulated chemotherapy regimens, dynamically adjusting doses based on real-time patient trajectories[7]. These adaptive approaches reduce the risk of over-treatment while maintaining efficacy.

Figure 6 shows integration of pharmacogenomics and patient data to optimize therapy and predict treatment response.

Notably, pharmacogenomic data integration has further advanced individualized dosing. ML models incorporating drug metabolism genes (e.g., TPMT, NUDT15) with prior toxicity events can forecast drug tolerance, guiding personalized protocols in children[6,23].

Despite progress, a key challenge remains the retrospective nature and limited cohort sizes of most studies. Prospective, multi-center trials and standardized methodologies are urgently required to translate these models into actionable bedside tools.

PRECISION THERAPY IN HAEMATOLOGICAL MALIGNANCIES

Precision therapy in haematological malignancies is increasingly driven by Machine Learning (ML), which enables individualized treatment selection, response prediction and monitoring of therapeutic resistance through integration of clinical, molecular, imaging and pharmacogenomic data. This data-driven approach supports optimized efficacy while minimizing treatment toxicity[24,25].

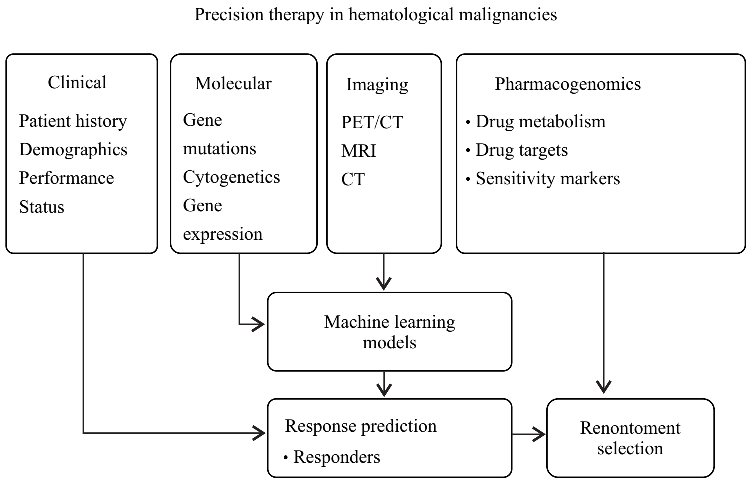

Fig. 7: Integrated ML pipeline using multi-modal data for individualized therapy in hematologic malignancies

Multi-modal data include clinical, molecular, imaging and pharmacogenomic inputs to support precision hematology

Table 1: Comparative applications of machine learning in haematological malignancies

Haematological malignancy	Early detection	Prognosis/risk stratification	Therapy/precision medicine
Leukaemia	CNN models for blast detection in blood smears; integration with flow cytometry data	Random forest/SVM for relapse prediction using mutational profiles (FLT3, NPM1)	Drug response prediction (cytarabine, TKIs); adaptive scheduling of chemotherapy
Lymphoma	Digital pathology for subtype classification (DLBCL, Hodgkin, Follicular); radiomics in PET/CT	ctDNA and gene expression-based relapse prediction; ML-enhanced IPI models	ML-guided prediction of CAR-T response; integration of clinical+ genomic data
Multiple Myeloma	ML-based plasma cell detection in bone marrow; integration of M-protein and FLC ratio	Prediction of progression from smoldering to symptomatic myeloma; cytogenetic abnormalities (del17p, t(4;14))	Response prediction to proteasome inhibitors (bortezomib, carfilzomib); MRD detection via ML

Figure 7 presents a pipeline integrating clinical, molecular, imaging and pharmacogenomic data for personalized treatment.

In Chronic Myeloid Leukemia (CML), ML models incorporating BCR-ABL transcript kinetics, cytogenetics and adherence data predict responses to tyrosine kinase inhibitors (imatinib, dasatinib, nilotinib), enabling early identification of non-responders and timely therapy adjustment24-25. In Acute Myeloid Leukemia (AML), ML frameworks integrating FLT3, NPM1 and cytogenetic markers forecast chemotherapy response, guiding intensified or targeted treatment strategies[8,25].

In lymphomas particularly Diffuse Large B-Cell Lymphoma (DLBCL), ML models combining clinical biomarkers, tumor microenvironment data and PET/CT metrics predict responders to CAR-T therapy versus standard immunochemotherapy, improving patient selection and toxicity risk management[26]. In multiple myeloma, ML predicts progression from smoldering to symptomatic disease and forecasts response to proteasome inhibitors, supporting earlier and more personalized intervention[27-29].

Despite these advances, most models remain retrospective and require prospective multi-center validation alongside ethical safeguards for bias, interpretability and data governance.

Table 1 summarizes the roles of ML in early detection, prognosis and therapy across leukemia, lymphoma and multiple myeloma.

CROSS-CUTTING APPLICATIONS OF MACHINE LEARNING IN HAEMATOLOGICAL MALIGNANCIES

Machine Learning (ML) is driving cross-cutting advances across haematological malignancies, particularly in measurable residual disease (MRD) detection, multi-omics integration and clinical decision support systems (CDSS), thereby transforming diagnostics, prognostication and therapeutic decision-making[30,31].

The ML enables cross-cutting applications, including MRD detection, multi-omics integration and decision support systems (Fig. 8).

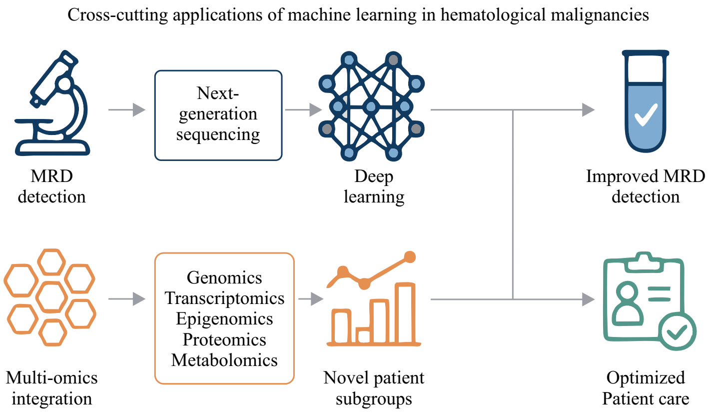

Fig. 8: ML-based framework for relapse prediction, risk stratification and personalized treatment planning in hematologic cancers
MRD: Minimal Residual Disease, CDSS: Clinical Decision Support System, multi-omics integrates genomic, transcriptomic and proteomic data

MRD detection: Next-Generation Sequencing (NGS) combined with deep learning enables ultra-sensitive MRD detection, identifying leukemic clones at levels approaching 10^{-6}, surpassing flow cytometry and qPCR sensitivity[32,33]. CNN-based sequence analysis detects rare variants and clonal evolution patterns, supporting earlier relapse prediction and post-remission therapy optimization[34].

Multi-omics integration: The ML platforms integrating genomic, transcriptomic, epigenomic, proteomic and metabolomic data reveal molecular subgroups with distinct prognostic and therapeutic profiles[8,35]. Such models improve relapse prediction in AML and progression risk stratification in multiple myeloma[29].

Clinical decision support systems: AI-driven CDSS provide real-time, patient-specific treatment recommendations by integrating clinical data, guidelines and predictive analytics supporting therapy selection, toxicity prediction and trial matching[25,36].

Despite the promise, challenges include limited prospective validation, data harmonization barriers, computational complexity and clinician adoption.

The application of machine learning in haematological malignancies, particularly acute lymphoblastic leukaemia (ALL) remains nascent but rapidly evolving. Priority efforts include building large, multi-center datasets to improve model generalizability and reduce institutional bias, supported by collaborative and federated learning frameworks that preserve data privacy. Standardized pipelines for data preprocessing, model training, validation and reporting are essential to ensure reproducibility and facilitate clinical adoption.

Integration with emerging technologies such as single-cell sequencing, spatial transcriptomics and liquid biopsy will enhance early detection and real-time disease monitoring. Coupling ML with electronic health records and clinical decision support systems can enable dynamic risk prediction, dose personalization, toxicity forecasting and relapse surveillance. Advancing explainable AI will be critical for clinician trust and interpretability of model outputs. Finally, adaptive regulatory pathways and strong ethical frameworks are required to guide safe, equitable implementation, particularly in low-resource settings. Collectively, these advances will position ML as a core pillar of precision oncology in ALL.

CONCLUSION

Machine learning is reshaping the management of haematological malignancies by strengthening diagnostics, prognostic modeling and therapy optimization. Deep learning enhances malignant cell detection and classification, while multi-omics-driven algorithms improve risk stratification, survival prediction and treatment response assessment. The ML also advances precision therapeutics through dose optimization, toxicity forecasting, drug-response modeling and improved decision-making in hematopoietic stem cell transplantation.

Despite these gains, clinical translation remains constrained by limited standardized datasets, insufficient external validation and workflow integration challenges. Ongoing progress in federated learning, multi-institutional data sharing and real-time clinical analytics is expected to address these gaps. As these barriers are overcome, machine learning will become central to precision oncology, enabling data-driven, reproducible and individualized care in haematological cancer management.

SIGNIFICANCE STATEMENT

This study highlights the transformative role of machine learning in improving the diagnosis, prognostication and treatment of haematological malignancies. It demonstrates how ML enhances diagnostic accuracy, reduces subjectivity and enables early disease detection beyond conventional methods. The work underscores the value of multi-omics integration for refined risk stratification and personalized therapy selection. It also emphasizes ML's potential to optimize treatment response, minimize toxicity and improve transplant outcomes. Importantly, the study addresses existing challenges to clinical translation, including data standardization and validation. Overall, it provides a strong evidence base supporting ML as a cornerstone of precision oncology in haematological cancer care.

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