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Machine Learning Applications in Schizophrenia: A Comprehensive Review

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Abstract

Schizophrenia is a severe and heterogeneous neuropsychiatric disorder characterised by complex symptoms, uncertain aetiology, and variable treatment outcomes. Traditional diagnostic methods relying on clinical observation and self-report often fail to capture the underlying biological diversity of the illness. Recent advances in machine learning (ML) have introduced powerful tools for analysing multimodal data and improving diagnostic precision, risk prediction, and treatment outcomes in schizophrenia. This comprehensive review summarises studies published between 2010 and 2025 that applied ML methods to schizophrenia across diverse data modalities, including neuroimaging, genomics, electronic health records, cognitive assessments, and digital phenotyping. Evidence shows that ML models, particularly deep learning and multimodal fusion techniques, can effectively distinguish schizophrenia from other psychiatric conditions, identify individuals at ultra-high risk for psychosis, predict treatment response, and uncover biologically meaningful subtypes. Despite these advances, major challenges remain, including small and imbalanced datasets, limited generalisability, model opacity, and ethical concerns related to privacy and bias. Addressing these limitations through large-scale, diverse datasets, explainable AI, and ethical frameworks will be essential for clinical translation. Integrating ML into psychiatric decision-support systems may enable earlier diagnosis, personalised treatment, and better long-term outcomes. With continued development and responsible implementation, ML holds the potential to transform schizophrenia care and advance the realisation of precision psychiatry.

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Introduction

Schizophrenia is a chronic, severe, and heterogeneous mental disorder that profoundly affects thought, perception, emotion, and behaviour.[1] It remains one of the most disabling psychiatric conditions worldwide, with significant clinical, social, and economic implications. The disorder's complex aetiology, encompassing genetic, neurodevelopmental, neurobiological, and environmental factors, creates challenges in achieving early and accurate diagnosis, predicting disease trajectory, and optimising treatment [2]. Traditional psychiatric assessments, which rely on clinical interviews and observable symptoms, often lack the precision needed to detect subtle biological markers or forecast individual responses to treatment. [3]

Current psychiatric assessments rely heavily on clinical interviews and behavioural observations, which are often useful, and clinical judgement, but typically lack the precision required to capture subtle biological signatures or prognostic information for an individual. These complex and multifaceted diagnostic problems have prompted researchers and clinicians to seek to employ computational methods and machine learning (ML) methods and analytic systems in psychiatric research, diagnosis, and treatment. Machine learning, which is a branch of artificial intelligence, refers to algorithms that can find hidden structures within high-dimensional data and use them to make predictions or classifications without programming the algorithm explicitly.[4] In psychiatry, machine learning has been increasingly utilised on multimodal data sources such as neuroimaging (structural and functional MRI, EEG), genomics, transcriptomics, electronic health records, and digital phenotyping data obtained from smartphones and wearables. Support vector machines (SVMs), random forests, logistic regression, ensemble learning, and deep learning architectures (e.g., convolutional neural networks and recurrent neural networks) have all demonstrated an ability to discriminate patients with schizophrenia from healthy controls, identify individuals at ultra-high risk for developing a psychotic disorder, and forecast their trajectory of treatment response or relapse.[5-9]

In addition to classification, unsupervised methods such as clustering and dimensionality reduction (including principal component analysis, t-SNE, and autoencoders) have been used to identify subtypes within schizophrenia and schizophrenia-related syndromes, adding evidence to suggest that psychiatric disorders occur on a continuous distribution as opposed to discrete categories[10,11]. Finally, supervised methods have also used natural language processing (NLP) to analyse (early) clinical notes and transcripts of speech and interactions on social media data to identify linguistically based early indications of psychosis[12-14]. Despite the advances in ML, there are important limitations to utilisation within psychiatry; small sample sizes or imbalanced datasets, high risk of overfitting, difficulty with complex and opaque inferences from the model, and limited generalizability are all important considerations with ML approaches in psychiatry. Furthermore, ethical considerations, including data privacy, algorithm-proof bias, and clinical accountability (i.e., clinical decisions based on ML), are points of consideration prior to implementation of ML into clinical practice[15-18].

ML refers to an assortment of algorithms that can identify underlying structures within high-dimensional data and make predictions or classify data without specific programming. In the field of psychiatry, ML has been employed increasingly with multimodal data sources, supporting analysis of complex data that may come from neuroimaging, genomics, clinical records, or digital phenotyping.[5,19-21] In general, ML approaches can be classified into three groups: supervised learning methods (e.g., support vector machines (SVMs), logistic regression, and random forests), unsupervised methods (e.g., clustering, principal component analysis (PCA), and autoencoders), and deep learning techniques (e.g., convolutional neural networks (CNNs), recurrent neural networks (RNNs), and transformers). Ensemble learning options (i.e., boosting and bagging) can help with prediction and improve performance by using multiple models.[22-32] A common workflow for all methods follows a similar pattern of data gathering, pre-processing, feature extraction, training and fine-tuning the model, and validating and evaluating the model. This framework is represented in most applications currently being conducted for psychiatric prediction.[15,33]

In recent years, advances in computational psychiatry and artificial intelligence (AI) have introduced new opportunities for understanding and managing schizophrenia. Among these, machine learning (ML)—a subset of AI that enables algorithms to identify patterns and make predictions from high-dimensional data without explicit programming—has shown substantial promise.[2,34,35] ML techniques have been applied across a range of data modalities, including neuroimaging, genomics, transcriptomics, electronic health records, cognitive assessments, and digital phenotyping from smartphones and wearable devices. These approaches have demonstrated the potential to differentiate patients with schizophrenia from healthy controls, identify individuals at high risk for psychosis, predict treatment response, and uncover biologically distinct subtypes.[2]

Despite encouraging results, several methodological and ethical challenges limit the clinical translation of ML in schizophrenia. These include small and imbalanced datasets, variability in data acquisition, limited model interpretability, and concerns regarding privacy, bias, and accountability. Addressing these challenges is critical for the responsible implementation of ML-driven tools in psychiatry. This review provides a comprehensive synthesis of current ML applications specifically in schizophrenia, summarising methodological advances, key findings, and ongoing challenges. It also highlights future directions aimed at developing interpretable, equitable, and clinically useful models that could transform schizophrenia care through precision psychiatry.

Methods

This review was conducted to summarise and critically evaluate current applications of ML in the prediction, diagnosis, and treatment of schizophrenia. A comprehensive literature search was performed in PubMed, Scopus, and Google Scholar for studies published between January 2010 and September 2025. The search terms included combinations of *"machine learning," "artificial intelligence," "deep learning," "neuroimaging," "genomics," "electronic health records," "digital phenotyping,"* and *"schizophrenia."*

Original research articles, systematic reviews, and meta-analyses focusing specifically on ML applications in schizophrenia were included. Studies exclusively addressing other psychiatric disorders were excluded unless they provided comparative insights relevant to schizophrenia. References of key publications were manually screened to identify additional eligible studies.

Extracted information included the ML technique used (e.g., support vector machines, random forests, convolutional neural networks), data modality (e.g., MRI, EEG, genetic, clinical, or behavioural data), study objectives, sample size, and key outcomes. Findings were organised thematically into major application areas—early risk identification, diagnostic classification, treatment response prediction, and clinical decision-support integration.

The review was structured following a narrative synthesis approach, highlighting methodological trends, limitations, ethical considerations, and emerging directions toward precision psychiatry in schizophrenia.

Result

Machine Learning Applications in Schizophrenia

ML has been increasingly applied in schizophrenia research to improve prediction, diagnosis, and treatment personalisation. Across multiple data modalities, neuroimaging, genomics, clinical records, and digital phenotyping, ML methods have demonstrated promising performance in identifying biomarkers and forecasting clinical outcomes.

Machine learning has been increasingly applied across different stages of psychiatric care, from early risk identification to treatment optimisation. These applications highlight the potential of ML to bridge the gap between research and clinical practice, enabling more precise and personalised care. Below are the key domains where ML has shown substantial promise.[36,37] One of the most critical applications of ML in psychiatry is the early identification of individuals at risk of developing schizophrenia or other psychotic disorders.[37,38]

Several studies have used ML algorithms such as support vector machines (SVMs), random forests, and deep learning networks to identify individuals at ultra-high risk (UHR) for psychosis. Models trained on structural and functional MRI data have predicted transition to schizophrenia with greater accuracy than traditional clinical assessments.[39]

Natural language processing (NLP) applied to speech and text data has detected early signs of thought disorder years before onset. Similarly, smartphone-based monitoring and digital phenotyping have revealed behavioural and social activity patterns indicative of early psychosis risk. Digital phenotyping: Smartphone-based monitoring of activity, mobility, and communication patterns has been used to identify behavioural shifts signalling early psychiatric deterioration.[40] By identifying at-risk individuals earlier, ML can support preventive interventions and reduce the duration of untreated psychosis, which is strongly linked to better long-term outcomes.

ML methods have also been applied to improve the accuracy of psychiatric diagnosis, which traditionally relies on subjective clinical evaluation. Subtyping within schizophrenia: Clustering and dimensionality reduction approaches have uncovered biologically distinct subgroups, such as patients with predominant cognitive impairment versus those with affective symptoms. Multimodal classification: Combining imaging, genomic, and clinical data has yielded robust classifiers capable of outperforming single-modality approaches.[41,42]

Improved classification supports the movement toward data-driven diagnostic frameworks and may inform future revisions of psychiatric nosology beyond the DSM/ICD categories.[43]

Predicting treatment outcomes remains one of the most challenging areas in psychiatry, where trial-and-error prescribing is common. ML has been applied to: Medication response: Models trained on clinical and genomic data have predicted which patients are likely to respond to specific antipsychotic medications (e.g., risperidone, clozapine), paving the way for personalised pharmacotherapy.[44–46]

Algorithms using genetic and metabolic profiles have estimated the risk of adverse effects, such as weight gain or extrapyramidal symptoms.[47]

Prognosis and relapse prediction: Longitudinal ML models leveraging EHRs, wearable sensor data, and social behaviour features have forecasted relapse events, hospital readmissions, and long-term functional outcomes.[48] These predictive tools can help clinicians personalise treatment plans, reduce unnecessary medication trials, and anticipate relapses before they occur. Beyond prediction, ML has contributed to understanding the biological mechanisms underlying schizophrenia and related disorders.[49]

Graph-theory-based ML approaches have revealed disrupted brain networks and altered connectivity hubs in schizophrenia, pointing toward dysconnectivity as a central feature of the disorder.[50,51] ML models applied to polygenic risk scores and gene expression data have identified pathways involved in synaptic signalling, immune function, and neurodevelopment as key contributors. Endophenotype discovery by clustering patients on the basis of cognitive, imaging, and genetic data, ML has uncovered intermediate phenotypes that may better explain heterogeneity in clinical presentation.[52,53]

These insights contribute to the shift from a purely symptom-based understanding of schizophrenia to a mechanistic, biology-informed perspective, which is essential for developing targeted therapies.[54]

Increasingly, ML applications are being integrated into comprehensive clinical decision-support systems (CDSS). These systems combine risk prediction, diagnostic classification, treatment response forecasting, and relapse monitoring into unified platforms. While still in early stages, pilot studies suggest that such systems may significantly aid psychiatrists in tailoring interventions, improving efficiency, and enhancing patient engagement.[55]

The effectiveness of machine learning to foresee and to classify schizophrenia and other mental disorders, to a great extent, relies upon the nature and the quality of the input data. Every modality provides one-of-a-kind clues, and nowadays a combination of modalities is being used not only for greater accuracy but also for wider understanding. [56-58]

Neuroimaging is still considered to be the most preferred data source in Machine Learning (ML) applications in psychiatry.[17,19] Some of the techniques used for this purpose are structural magnetic resonance imaging (sMRI), functional MRI (fMRI), diffusion tensor imaging (DTI), and electroencephalography (EEG), which provide biomarkers of brain structure, connectivity, and activity.[59-65] Through sMRI, several changes have been reported, such as cortical thinning, reduction of gray matter, and volumetric abnormalities associated with schizophrenia.[66,67] ML models like support vector machines (SVMs) and random forests have been utilised to perform the classification of patients vs. healthy controls by using these structural features as a basis. fMRI measures resting-state and task-related functional connectivity patterns. Therefore, models such as convolutional neural networks (CNNs) and graph-based learning methods can support the identification of disrupted brain networks that are potentially linked to psychosis. DTI has been utilised to examine white matter integrity, while ML algorithms have pointed out the microstructural changes in tracts like the corpus callosum. EEG/MEG offers high temporal resolution, and the use of recurrent neural networks (RNNs) and temporal pattern recognition techniques has made it possible to identify abnormal oscillatory activity that predicts the occurrence of schizophrenia.[66-70]

Genomic data provide another powerful perspective, shedding light on the heritability and biological roots of psychiatric disorders. Genome-wide association studies (GWAS)[71] have identified numerous single-nucleotide polymorphisms (SNPs) associated with schizophrenia risk. ML approaches such as regularised regression models (LASSO, elastic net) and ensemble methods have been used to construct polygenic risk scores that improve risk prediction. Transcriptomic and epigenetic data have also been analysed with deep learning models like autoencoders, uncovering genetic signatures tied to psychiatric outcomes. Integrating genomic data with imaging and clinical features is an emerging and promising direction.[72–76]

Electronic health records (EHRs) offer rich, longitudinal clinical information, including diagnoses, treatments, and hospital admissions. Natural language processing has been applied to unstructured notes, allowing the early identification of psychosis risk factors. ML models trained on EHR data have also shown promise in predicting hospital readmissions, treatment adherence, and relapse risk.[74,77–79]

Behavioural and cognitive assessments, such as psychometric tests and structured interviews, further support classification tasks. ML models built on these inputs have successfully distinguished schizophrenia disorders.[80]

Digital phenotyping, enabled by smartphones and wearable devices, has emerged as a novel and rapidly growing data source. Passive measures like GPS tracking, call/text activity, and screen time can reveal patterns of social withdrawal, cognitive impairment, or circadian rhythm disruptions, which are common in schizophrenia.[81] Additionally, speech and language analysis through NLP and acoustic methods has proven effective in detecting early markers of thought disorder and predicting psychosis onset. Social media data, including posting behaviour and language use, have also been studied, though concerns about privacy remain significant.[82]

Because schizophrenia is highly heterogeneous, relying on a single data source often proves insufficient.[81,83] Recent research highlights the benefits of multimodal approaches, which combine neuroimaging, genomic, clinical, and digital data. Methods such as multimodal deep learning, feature fusion, and ensemble modelling consistently outperform single-modality approaches. For example, combining fMRI connectivity data with genomic risk scores has improved classification accuracy, while integrating EHR and digital phenotyping has enhanced relapse prediction.[81–86]

Discussion

While machine learning has shown significant promise in predicting schizophrenia, several methodological and practical challenges limit its clinical translation. These challenges span issues related to data, model development, interpretability, reproducibility, and real-world deployment.[87]

Many datasets have skewed class distributions (e.g., far fewer individuals who transition from high-risk to schizophrenia compared to those who do not). Imbalanced data can bias models toward the majority class, leading to poor sensitivity for clinically critical outcomes like relapse or psychosis onset.[88]

Schizophrenia is inherently heterogeneous, and data collection protocols vary widely across studies, scanners, and clinical settings. Lack of standardisation complicates model training and reduces generalizability across populations. Missing data, noise in electronic health records, motion artefacts in neuroimaging, and incomplete genomic datasets are common. ML models trained on noisy data risk producing unreliable outputs.[88,89]

Overly complex models (e.g., deep neural networks with many parameters) may fit the idiosyncrasies of a training dataset rather than true underlying patterns. Without rigorous external validation, such models often fail when applied to new populations.[90]

Unlike in computer vision or natural language processing, psychiatry lacks large benchmark datasets and standardised evaluation frameworks. This makes it difficult to compare models across studies and slows scientific progress. Many studies report high accuracy on internal datasets but fail to replicate results in independent cohorts. Variability in pre-processing pipelines, feature extraction methods, and performance metrics contributes to this problem. Deep learning models often achieve high accuracy but provide little insight into how predictions are made. In psychiatry, where clinical decisions can have profound consequences, the lack of transparency is a major barrier to adoption.[91,92]

Many ML studies in psychiatry are based on data from Western, educated, industrialised, rich, and democratic (WEIRD) populations. Models trained in such contexts may not generalise to diverse cultural or socioeconomic settings, raising concerns about bias and inequity. Variability in scanner hardware, imaging protocols, and clinical diagnostic practices introduces systematic differences that can degrade model performance when applied across sites.[91,93,94]

Psychiatric data is highly sensitive. ML applications relying on digital phenotyping, EHRs, or social media raise concerns about privacy breaches and informed consent. Biased training data can lead to unfair predictions, for instance, overdiagnosing or underdiagnosing certain demographic groups. This exacerbates existing disparities in mental health care. Determining responsibility for decisions made with ML support remains unclear, whether the clinician, institution, or algorithm developer should be accountable for adverse outcomes. Few ML-based psychiatric tools have passed through rigorous regulatory approval processes (e.g., FDA, EMA), limiting their availability in clinical practice.[49,88,90–92,95]

Ethical, Legal, and Social Considerations

The integration of machine learning into psychiatry introduces not only technical and methodological challenges but also a range of ethical, legal, and social issues. Because psychiatric data is deeply personal and stigmatised, these challenges must be carefully addressed to ensure that the benefits of ML are realised without compromising patient rights, equity, or trust in mental health systems.[49,93,95]

Unlike many other medical domains, psychiatric data often contains subjective accounts of thoughts, emotions, and behaviours, which are particularly vulnerable to misuse. For example, digital phenotyping through smartphone monitoring captures intimate behavioural patterns such as sleep cycles, mobility, and social interactions.[52,93]

Storing and processing psychiatric data, especially when linked across modalities (EHRs, neuroimaging, genomics, and digital behaviour), raises the risk of breaches that could expose sensitive information. Strong encryption, federated learning (where data never leaves the local institution), and anonymisation are necessary to ensure secure handling of psychiatric data.[92,93]

Many ML applications rely on continuous data collection from smartphones or wearables. Patients may not fully understand the scope of data being collected or how it will be used. Continuous digital tracking raises questions about whether patients truly have the option to opt out without feeling coerced, particularly in clinical or institutional settings. Emerging frameworks propose allowing patients to update or withdraw consent in real time, thereby preserving autonomy and trust.[55,88,95]

Model Interpretability and Clinical Trust

Deep learning models, though powerful, often function as “black boxes,” offering little explanation for their predictions. Clinicians require interpretable models that highlight key features—such as specific brain regions or genetic markers—to build confidence in their use. Techniques like SHAP values, attention mechanisms, and explainable AI are being explored but remain underused in psychiatric research.[96]

When ML models are used to inform diagnosis or treatment, questions arise about who is accountable for errors: the clinician, the healthcare institution, or the algorithm developers. Most argue that ML should be a decision-support tool rather than an autonomous decision-maker in psychiatry. However, even in supportive roles, reliance on ML outputs could shift responsibility in ambiguous ways.[96,97]

Regulatory agencies such as the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) have begun developing frameworks for AI/ML in healthcare. However, few psychiatric applications have yet undergone formal regulatory approval.[98]

Predictive tools that label individuals as "high risk" for schizophrenia could unintentionally increase stigma or discrimination in employment, insurance, and education. Access to ML-driven tools (e.g., mobile health apps, wearable sensors) may be limited in low-resource settings, potentially widening existing inequities in mental health care.[97]

Transparency, interpretability, and clear communication of model limitations are essential to build trust among patients, clinicians, and the public. Without trust, adoption of ML in psychiatry will remain limited.[98]

Future Directions and Opportunities

Progress in large-scale, multi-site collaborations such as ENIGMA and PsychENCODE will support the development of more representative datasets. Integrating multimodal data—neuroimaging, genetics, EHR, and digital behaviour—using advanced fusion models may enhance accuracy and reveal new schizophrenia subtypes. The next generation of ML research must prioritise fairness-aware algorithms, explainability, and transparency to facilitate regulatory approval and clinician adoption. Embedding ML tools within clinical decision-support systems could help realise the promise of precision psychiatry, offering earlier diagnosis, individualised treatment, and improved patient outcomes.

Conclusion

Schizophrenia remains one of the most complex and disabling psychiatric disorders, with challenges in early detection, diagnosis, and treatment prediction. Machine learning (ML) has emerged as a transformative approach capable of analysing high-dimensional, multimodal data to reveal hidden biological and behavioural patterns underlying the illness. Evidence from neuroimaging, genomic, and digital phenotyping studies demonstrates that ML can enhance diagnostic precision, predict treatment outcomes, and support the development of personalised interventions. However, the field still faces critical barriers, including small and heterogeneous datasets, limited model interpretability, and ethical concerns related to privacy and bias. Future research must prioritise large, diverse, and longitudinal datasets alongside explainable and ethically responsible AI frameworks. With continued innovation and clinical integration, ML holds significant promise for advancing precision psychiatry and improving long-term outcomes for individuals with schizophrenia.

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