

REVIEW ARTICLE

A Systematic Review of Predictive Modeling and Personalized Interventions in the Clinical Management of Opioid Use Disorder



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Publication history: Received on 24th January 2026; Revised on 5th March 2026; Accepted on 6th March 2026

Article DOI: 10.69613/6ba84639

Abstract: Opioid Use Disorder (OUD) is characterized by chronic relapse, high mortality rates, and significant socioeconomic burdens. Conventional clinical methods often struggle with diagnostic delays and the inability to provide real-time, personalized monitoring. The integration of Artificial Intelligence (AI) and Machine Learning (ML) into addiction medicine offers a transformative pathway for optimizing patient outcomes. Through the deployment of sophisticated algorithms ranging from logistic regression and random forests to gradient boosting and deep neural networks clinicians can now leverage large-scale datasets, including electronic health records and wearable sensor data, to predict overdose risks and individual treatment responses with high precision. These computational models facilitate early risk stratification, enabling proactive interventions before the onset of severe dependency or life-threatening events. The application of natural language processing and reinforcement learning allows for the dynamic adjustment of pharmacotherapeutic and psychosocial protocols, moving the field toward a precision medicine framework. Despite these advancements, the clinical utility of AI is currently moderated by challenges related to data heterogeneity, algorithmic transparency, and ethical considerations regarding patient privacy and bias. Effective integration into the broader healthcare ecosystem requires standardized validation protocols and collaborative efforts between data scientists and clinicians. Addressing these systemic barriers is essential for the realization of a data-driven approach to addiction recovery that reduces relapse rates and enhances long-term survivability for affected populations.

Keywords: Computational Psychiatry; Addiction; Neural Networks; Predictive Analytics; Precision Healthcare.

1. Introduction

Opioid Use Disorder (OUD) is a chronic, relapsing condition defined by the compulsive seeking and consumption of opioid substances despite the presence of significant adverse biological and social consequences. The disorder is classified within the broader spectrum of substance use disorders (SUD) and is physiologically marked by the development of tolerance, physical dependence, and a debilitating withdrawal syndrome upon cessation of the substance [1]. The transition from recreational use or pain management to a disordered state involves complex neurobiological adaptations, particularly within the mesolimbic reward system and the prefrontal cortex. These changes lead to a profound dysregulation of decision-making processes and the reinforcement of maladaptive behavioral patterns [2]. Genetic predispositions, environmental stressors, and psychological vulnerabilities converge to facilitate the neuroplastic changes that characterize the state of addiction, making OUD a multifaceted challenge for modern clinical practice.

The scale of the opioid crisis is reflected in global statistics provided by major health organizations. Current estimates suggest that over 27 million individuals worldwide are living with opioid use disorders, and opioids contribute to approximately 70% of all drug-related fatalities [2]. The annual mortality rate associated with opioid overdose is approximated between 125,000 and 130,000 deaths globally [2]. In the United States, the crisis reached unprecedented levels by 2020, with nearly 2 million Americans diagnosed with OUD [3]. The Centers for Disease Control and Prevention documented more than 70,000 drug-induced deaths in a single year, with the vast majority involving synthetic opioids such as fentanyl [3]. The proliferation of these potent synthetic agents, combined with historical over-prescription of analgesic opioids and the availability of illicit heroin, has accelerated the incidence of fatal respiratory depression and long-term disability [1].

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Diagnosing OUD remains inherently difficult due to the overlapping symptoms shared with other psychiatric conditions and chronic pain syndromes [4]. Societal stigma and the fear of criminalization often prevent individuals from disclosing their usage patterns to healthcare providers, leading to significant underreporting and delayed therapeutic engagement [5]. Standard treatment modalities, which typically combine Medication-Assisted Treatment (MAT) including buprenorphine, methadone, or naltrexone with psychosocial therapies like cognitive-behavioral therapy, face substantial logistical hurdles. Treatment gaps are particularly pronounced in rural and underserved regions where specialized addiction facilities are scarce. The high rate of relapse, estimated to occur in 40% to 60% of patients following the initial treatment phase, indicates that static treatment models are insufficient for managing the dynamic nature of addiction [1, 5]. There is a critical need for adaptive, data-driven tools that can identify at-risk individuals and provide continuous monitoring throughout the recovery process.

2. Predictive Modeling in OUD

2.1. Linear and Logistic Modeling

The foundational application of machine learning in addiction medicine often begins with logistic regression due to its high degree of interpretability and ease of clinical integration. In the context of OUD, logistic regression is frequently utilized for binary classification tasks, such as determining the probability that a patient will transition from acute pain management to chronic opioid misuse [6]. These models operate on structured datasets, analyzing variables such as prescription history, demographic factors, and the presence of comorbid psychiatric diagnoses to generate a risk probability score [7]. While less complex than modern deep learning architectures, the transparency of logistic regression allows clinicians to identify specific risk factors, which is paramount in environments where the explainability of a decision directly affects patient trust and regulatory compliance.

2.2. Ensemble Learning and Decision Structures

To address the nonlinear relationships inherent in addiction data, ensemble methods such as Decision Trees and Random Forests have become prominent. Decision trees provide a hierarchical framework for risk stratification by recursively partitioning data based on feature thresholds, such as the morphine milligram equivalent (MME) dosage or the frequency of emergency department visits. Random Forests enhance this approach by aggregating the outputs of multiple decision trees, thereby reducing the risk of overfitting and improving the robustness of the predictions [7]. These models are particularly effective at identifying individuals at risk for sustained opioid use or overdose. A significant clinical advantage of tree-based models is the provision of feature importance rankings, which allow researchers to pinpoint high-impact predictors like the co-prescription of benzodiazepines or specific social determinants of health that contribute to the likelihood of relapse.

Table 1. Comparison of Computational Models in OUD Management

Model Architecture	Core Mechanism	Primary Strengths	Clinical Use Case
Logistic Regression	Linear probability estimation	High interpretability; ease of deployment	Initial risk scoring in EHR systems [6, 7]
Random Forests	Ensemble of decision trees	Handles non-linear data; provides feature importance	Identifying predictors of dose escalation [7]
Gradient Boosting (XGBoost/LightGBM)	Iterative error minimization	Superior predictive accuracy; robust to missing data	Overdose prediction in large cohorts [8]
Support Vector Machines (SVM)	Hyperplane classification	Effective in high-dimensional feature spaces	Classifying behavior patterns in small datasets [9]
Recurrent Neural Networks (RNN/LSTM)	Sequential data processing	Captures temporal dependencies and trajectories	Predicting relapse using time-series sensor data [10]

2.3. Gradient Boosting and High-Dimensional Optimization

Gradient Boosting Machines (GBM), including advanced implementations like XGBoost and LightGBM, represent a more sophisticated class of ensemble learning that focuses on minimizing prediction errors through iterative optimization. In OUD research, these algorithms are employed to analyze massive, high-dimensional clinical datasets where traditional statistical methods may fail to capture subtle interactions between variables [8]. Gradient boosting achieves superior accuracy in predicting incident OUD cases and overdose events by sequentially building models that address the residuals of previous iterations. These architectures are particularly resilient to the missing data frequently encountered in longitudinal electronic health records, making them suitable for real-world clinical applications where data completeness is often suboptimal [8].

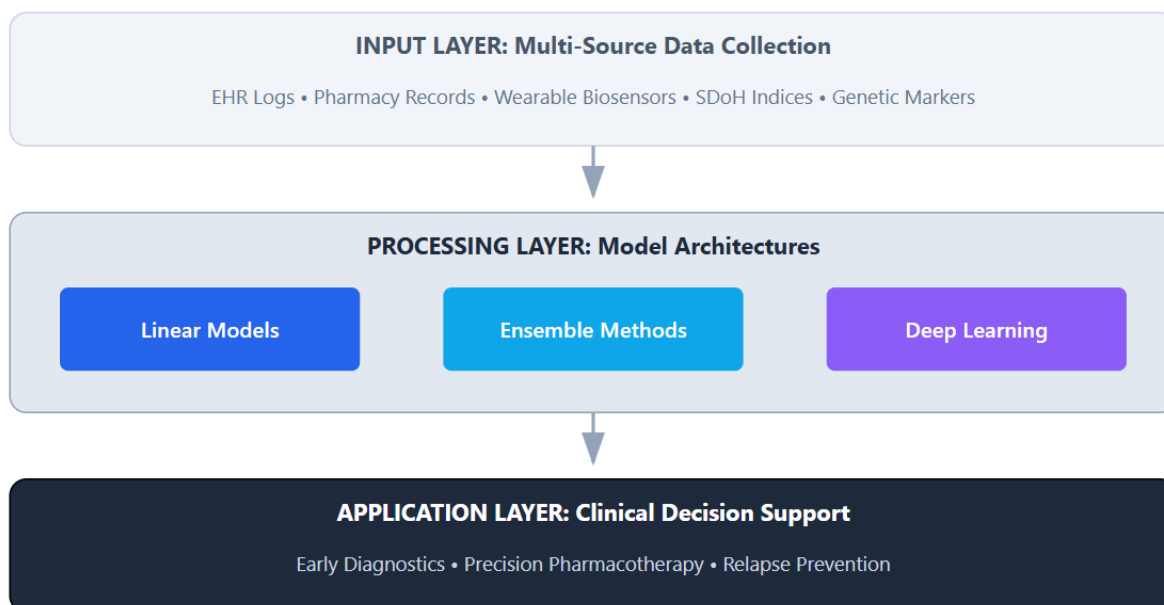


Figure 1. Processing layers from raw data input to decision support of ML Models in OUD

2.4. Support Vector Machines and Kernel-Based Classification

Support Vector Machines (SVM) offer a powerful mechanism for classification in high-dimensional feature spaces, utilizing kernel functions to separate complex data points that are not linearly separable. In the management of opioid dependency, SVMs have been applied to categorize patients into distinct risk groups and to differentiate between various patterns of substance use behavior based on physiological and behavioral inputs [9]. While SVMs are highly effective at finding optimal boundaries between high-risk and low-risk cohorts, they are often viewed as "black boxes" compared to decision trees, as the specific logic behind a classification can be difficult for a clinician to interpret. Nevertheless, their ability to handle small but complex datasets makes them a valuable tool for specialized pilot studies and pilot interventions.

2.5. Deep Learning and Temporal Analysis

Recent advancements in deep learning, particularly the use of Recurrent Neural Networks (RNNs) and Long Short-Term Memory (LSTM) networks, have enabled the analysis of temporal sequences in patient data. These architectures are uniquely capable of processing longitudinal records to identify trajectories of use that precede a relapse or overdose [10]. Deep learning models provide a predictive window that allows for early clinical intervention by learning the patterns of "stress spikes" or physiological changes over time. The integration of these models with mobile health platforms ensures that patient monitoring is not restricted to the clinical setting but extends into the daily environment where triggers for substance use are most prevalent.

3. Clinical Applications in Management Interventions

3.1. Risk Assessment and Predictive Screening

The deployment of risk-stratification algorithms represents a critical shift from reactive to proactive addiction medicine. These systems synthesize multidimensional patient data, including demographic profiles, longitudinal substance use histories, and the presence of high-risk co-prescriptions such as benzodiazepines or gabapentinoids, to generate individualized risk indices. Clinical studies demonstrate that machine learning models can identify patients at high risk of developing OUD following an initial opioid prescription for acute pain with an accuracy exceeding 80% [11]. Clinicians receive real-time alerts that facilitate earlier preventive measures by integrating these scores into the electronic health record (EHR) interface such as the implementation of more stringent monitoring protocols or the transition to non-opioid analgesic alternatives. The capacity of these models to detect "hidden" misuse patterns often characterized by subtle changes in healthcare utilization or appointment adherence allows for clinical engagement before the progression to a severe disorder [11, 12].

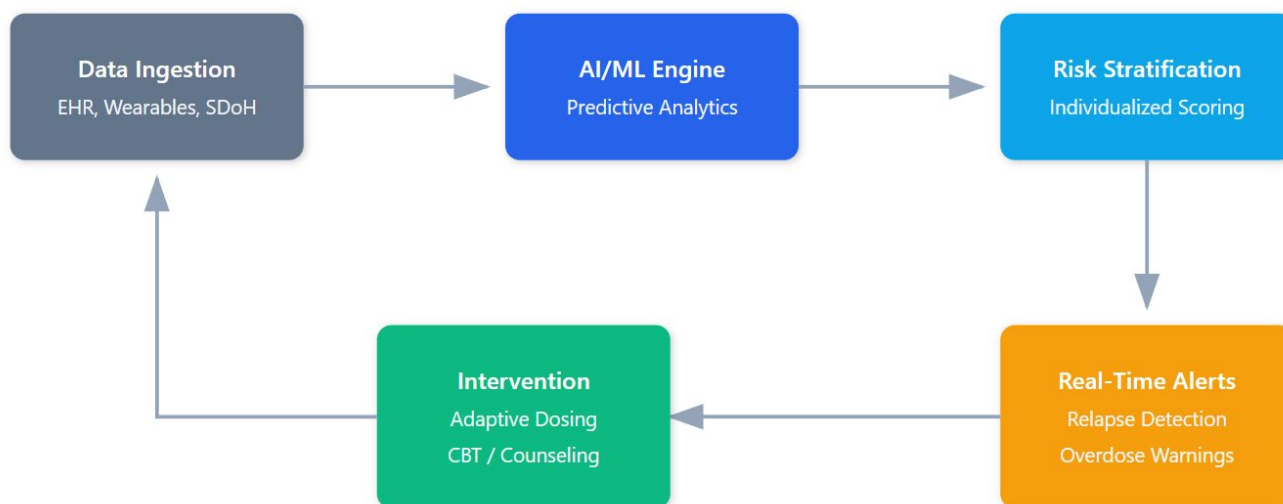


Figure 2. AI-Integration for the Management of OUD

Table 2. Multidimensional Data Features for Predictive Risk Stratification

Feature Category	Specific Variables/Indicators	Rationale for Inclusion
Clinical History	Prior SUD diagnosis; comorbid psychiatric disorders (Anxiety/Depression)	High correlation with vulnerability to opioid dependency [1, 4]
Pharmacological	Morphine Milligram Equivalents (MME); Benzodiazepine co-prescription	Established biological risk factors for respiratory depression [11]
Healthcare Utilization	Frequency of ED visits; "doctor shopping" patterns; missed appointments	Behavioral indicators of escalating misuse or instability [12]
Socioeconomic (SDoH)	Employment status; housing stability; ZIP-level deprivation index	External stressors that influence treatment retention and relapse [13]
Biometric/Physiological	Heart rate variability (HRV); sleep architecture; SpO2 levels	Real-time indicators of craving or acute withdrawal [14,15]

3.2. Precision Pharmacotherapy and Adaptive Dosing

One of the most impactful transitions in OUD management is the movement toward precision medicine, which seeks to move beyond the standardized administration of methadone or buprenorphine. Computational models now leverage genetic polymorphisms, specifically those affecting the mu-opioid receptor (OPRM1) and metabolic enzymes like CYP2D6, to predict an individual's response to different Medication-Assisted Treatment (MAT) agents [13]. AI systems can recommend the specific pharmacotherapeutic agent and starting dosage most likely to achieve early stabilization by clustering patients into clinically relevant subgroups based on their neurobiological and behavioral profiles. Reinforcement learning algorithms provide a framework for adaptive dosing, where the treatment plan is dynamically modified based on the patient's physiological feedback and self-reported craving intensity [14, 15]. This iterative optimization addresses the chronic and relapsing nature of OUD by ensuring that the pharmacological support remains aligned with the patient's current clinical state.

3.3. AI-Augmented Psychosocial and Behavioral Interventions

Beyond the biological aspects of addiction, computational intelligence is being applied to enhance the efficacy of behavioral therapies. Natural Language Processing (NLP) techniques allow for the objective analysis of therapeutic discourse, identifying linguistic markers of emotional distress or impending relapse within counselor notes or patient-provider communications [15]. These insights enable the delivery of personalized counseling techniques, such as cognitive-behavioral therapy (CBT) modules tailored to the specific triggers identified by the algorithm. Virtual support systems, including AI-driven chatbots, provide a continuous presence for patients between clinical visits, offering immediate coping techniques during periods of high craving. Empirical data suggests that such virtual interventions can lead to a significant reduction in opioid cravings and improved adherence to long-term recovery goals by providing a non-judgmental and readily accessible support mechanism [16].

4. Real-Time Monitoring and Prevention of Recurrence

4.1. mHealth Architectures and Wearable Sensors

The integration of wearable technology and mobile health (mHealth) applications provides a continuous stream of physiological data that was previously inaccessible in traditional clinical settings. Sensors capable of tracking heart rate variability, sleep architecture, and peripheral oxygen saturation offer a proxy for the patient's autonomic and respiratory state. Machine learning models trained on these biometrics can detect the early physiological signs of opioid self-administration or the onset of withdrawal symptoms with high sensitivity [17]. For example, random forest classifiers have been successfully utilized to differentiate between physiological stress and the specific respiratory depression associated with opioid consumption. This real-time visibility allows for the deployment of "just-in-time" adaptive interventions, where a patient or caregiver is alerted the moment a deviation from the healthy baseline is detected, potentially preventing fatal overdose events [17, 18].

Table 3. Wearable Sensor Modalities for Real-Time OUD Monitoring

Sensor Type	Physiological Marker	Clinical Relevance in OUD
Photoplethysmography (PPG)	Heart Rate (HR) / HRV	Detects sympathetic nervous system arousal during craving/stress [18]
Pulse Oximetry (SpO ₂)	Blood oxygen saturation	Essential for detecting opioid-induced respiratory depression [17]
Actigraphy	Physical activity / Sleep cycles	Identifies restlessness or insomnia associated with withdrawal [18]
Electrodermal Activity (EDA)	Skin conductance / Sweat	Measures acute stress responses and physiological triggers [17]

4.2. Predictive Analytics for Relapse and Overdose Detection

Relapse remains the most significant hurdle in the recovery trajectory, often occurring with little warning for the clinical team. Advanced predictive models now combine physiological data from wearables with ecological momentary assessments (EMA) short, frequent surveys delivered via smartphone to capture the patient's psychological state in their natural environment. These models achieve an accuracy of approximately 82.6% in predicting recurrence by identifying "stress spikes" and changes in behavioral patterns 24 to 48 hours prior to a potential relapse event [18]. This predictive window is crucial for clinical intervention, enabling the provision of additional social support or pharmacological adjustments before the patient resumes substance use. In the event of an overdose, AI systems integrated with wearable devices can automatically trigger emergency responses, such as alerting first responders or nearby individuals equipped with naloxone, thereby reducing the time to life-saving treatment [11, 18].

4.3. Public Health Surveillance and Community-Level Interventions

At the macro level, machine learning provides powerful tools for public health surveillance and the careful allocation of resources. AI models can identify geographic "hotspots" of opioid misuse and clusters of overdose fatalities by analyzing population-level data, including emergency department records, pharmacy dispensing logs, and law enforcement reports. These insights allow public health officials to deploy harm reduction programs, such as naloxone distribution and mobile treatment clinics, to the areas of greatest need with unprecedented precision. Predictive modeling at the community level helps in identifying gaps in treatment access and informing policy decisions regarding the expansion of recovery services in underserved or rural regions. This data-driven approach ensures that the systemic response to the opioid crisis is both efficient and responsive to the evolving landscape of the epidemic [12, 19].

Table 4. Synthesis of Empirical Evidence from Clinical AI/ML Studies

Study (Year)	Algorithm(s) Used	Population Size (N)	Primary Metric/Outcome
Banks et al. (2023)	Gradient Boosting / RF	1,200 (ED encounters)	80% accuracy in detecting hidden misuse patterns [11]
Faysal et al. (2026)	GBM & Elastic Net	182,083 (EHR)	C-statistic 0.879 for predicting incident OUD [8]
Mahoney et al. (2023)	Multi-modal ML	77 (Longitudinal)	82.6% accuracy in predicting relapse 24h in advance [18]
Balise et al. (2026)	Deep Learning	~5,000	Optimization of buprenorphine vs. methadone efficacy [13]
Baker et al. (2020)	NLP / Chatbot (Suzy)	84	25% reduction in self-reported opioid cravings [16]

5. Challenges and Ethical Limitations

5.1. Data Integrity and Algorithmic Bias

The efficacy of computational models in managing OUD is fundamentally constrained by the quality and representative nature of the underlying datasets. Electronic Health Records (EHR) often contain significant noise due to inconsistent clinical coding, missing longitudinal data, and variations in institutional documentation practices [20]. Such irregularities can introduce systematic errors, leading to the misclassification of high-risk patients or the generation of "false alarms" that contribute to alert fatigue among clinicians. The lack of diversity in training datasets poses a significant risk of algorithmic bias. If models are predominantly trained on data from urban populations or specific socioeconomic strata, their predictive accuracy may diminish when applied to marginalized groups or rural communities [21]. Given that OUD disproportionately affects vulnerable populations, ensuring that AI applications are trained on inclusive datasets is a prerequisite for equitable healthcare delivery [21, 22].

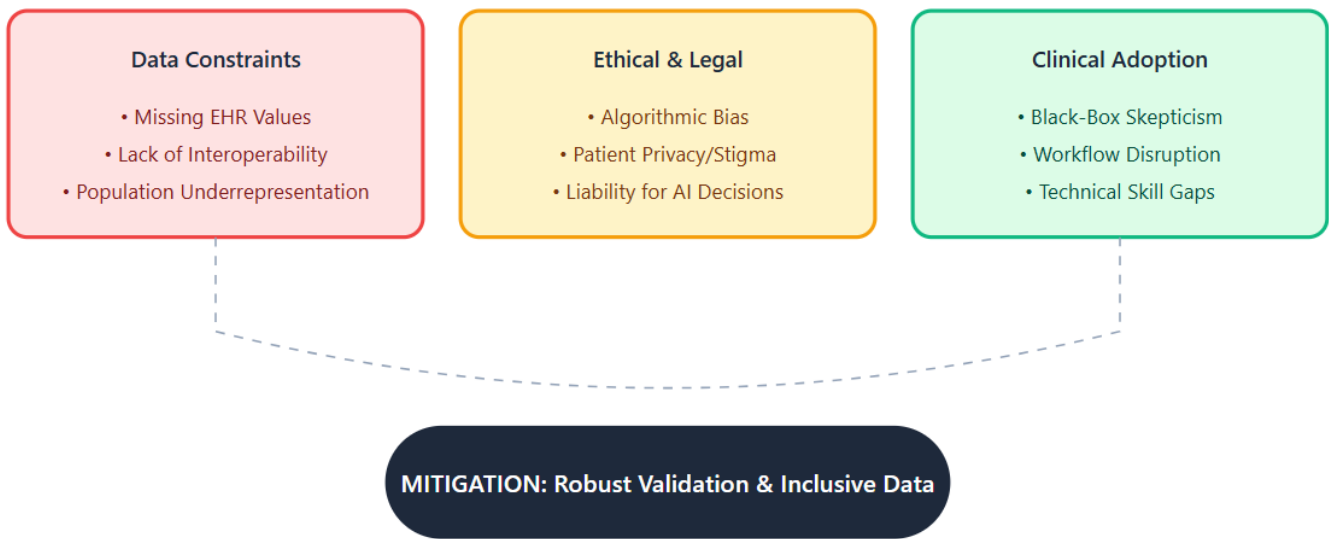


Figure 3. Barriers of Systemic, ethical, and clinical challenges limiting AI adoption.

Table 5. Challenges and Computational Mitigation Methods

Challenge Category	Specific Limitation	AI/ML Mitigation Techniques
Data Quality	Missing values and noise in EHR clinical notes	Use of NLP and Imputation algorithms to enhance data density [20, 23]
Algorithmic Bias	Lower accuracy in marginalized or rural populations	Fairness-aware learning and diverse data oversampling [21, 22]
Interpretability	"Black box" nature of deep learning	Integration of SHAP or LIME for local feature explanation [6, 23]
Model Drift	Declining accuracy as drug use patterns evolve	Continuous learning loops and periodic model re-calibration [24]

5.2. Privacy, Stigma, and Legal Liability

The sensitivity of addiction-related data necessitates rigorous adherence to privacy standards and data protection protocols. Unauthorized access to information regarding a patient's substance use history can lead to severe social stigma, employment discrimination, or legal repercussions. While AI models require large-scale data sharing to improve their predictive capabilities, this must be balanced against the patient's right to confidentiality [20, 22]. Additionally, the integration of AI into clinical workflows introduces complex questions regarding medical liability. In instances where an algorithmic recommendation leads to an adverse outcome such as an incorrect dosage adjustment or a missed relapse warning determining whether responsibility lies with the clinician, the healthcare institution, or the software developer remains a significant legal challenge that currently lacks standardized regulatory frameworks [22, 23].

5.3. Implementation Barriers in Clinical Workflows

The practical adoption of AI tools is often hindered by the technological inertia of existing healthcare infrastructures. Many addiction treatment centers operate on legacy systems that lack the interoperability required for real-time data processing. There is a notable "trust gap" among healthcare professionals regarding the "black box" nature of complex deep learning models [23]. Clinicians may be reluctant to rely on suggestions from an algorithm if the underlying logic is not transparent or clinically intuitive. Overcoming these barriers requires a significant investment in both technical infrastructure and specialized training for medical personnel to ensure that computational tools augment, rather than disrupt, the therapeutic alliance between the patient and the provider [23, 24].

6. Future Scope

6.1. Multi-Omics and Precision Diagnostics

The next generation of computational intelligence in OUD will likely focus on the integration of multi-omics data incorporating genomics, transcriptomics, and metabolomics with behavioral and clinical records. This holistic approach will enable the identification of highly specific biological markers that correlate with treatment resistance or vulnerability to relapse [25, 26]. AI can facilitate a transition toward a truly individualized diagnosis by analyzing these intricate datasets where therapeutic choices are dictated by the patient's unique biological signature. Such advancements are expected to significantly reduce the trial-and-error period currently associated with finding effective pharmacological stabilization for OUD [26, 27].

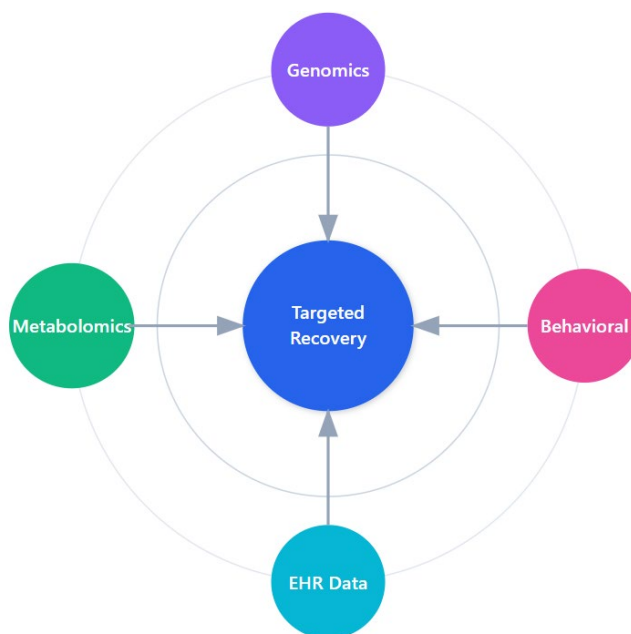


Figure 4. Convergence of biological and behavioral data into targeted OUD Recovery

Table 6. Future Scope for AI in OUD

Phase	Objective	Technologies
Short-Term	EHR integration of risk alerts	API-based CDS tools; Logistic/Tree models
Medium-Term	Dynamic recovery support	AI chatbots; Reinforcement learning for adaptive dosing
Long-Term	Precision Addiction Medicine	Multi-omics integration; Federated learning for privacy
Policy Level	Standardized Validation	Algorithmic auditing; Ethical AI regulatory frameworks

6.2. Collaborative Public Health Ecosystems

The evolution of addiction management requires the seamless integration of AI-driven tools into a broader, multi-disciplinary healthcare ecosystem. This involves creating standardized data formats that allow for the secure exchange of information between emergency services, mental health clinics, and long-term recovery programs [28]. Future policy-making should focus on establishing clear guidelines for the validation and auditing of algorithms used in OUD care to ensure fairness and clinical safety. Collaborative

frameworks between policymakers, data scientists, and clinicians will be essential for transforming computational insights into sustainable public health interventions that address both the individual and community-level impacts of the opioid crisis [28, 29].

7. Conclusion

The integration of Artificial Intelligence and Machine Learning into the management of Opioid Use Disorder represents a paradigm shift in addiction medicine. By transitioning from static, population-level protocols to dynamic, data-driven interventions, these technologies offer the potential to significantly improve early detection, personalize pharmacological treatment, and provide continuous, real-time monitoring. Evidence suggests that sophisticated algorithms can identify high-risk usage patterns and predict relapse events with a level of precision that exceeds traditional clinical assessment. However, the realization of this potential depends on addressing critical systemic issues, including data quality, algorithmic bias, and the ethical management of sensitive patient information. As computational models become more sophisticated and integrated into clinical workflows, they will serve as indispensable tools in reducing the global burden of OUD, ultimately enhancing patient survivability and the long-term success of recovery programs.

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