WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL RESEARCH

Review Article

Coden USA: WJPPCL

2026
Volume: 03
Issue: 06
Page: 134-142

REVIEW ON AI IN DRUG SAFETY AND EFFICACY ASSESSMENT

Pawan Patidar*, Mrs. Kajal Mudgal

Mandsaur Institute of Pharmacy, Mandsaur University.

Received: 21 April 2026 **Revised: 11 May 2026** **Accepted: 31 May 2026**

Corresponding Author: Pawan Patidar

Address: Research Scholar, Mandsaur Institute of Pharmacy, Mandsaur University, Mandsaur.

DOI: https://doi.org/10.5281/zenodo.20483822,

ABSTRACT

This review discusses the application of AI in drug safety and efficacy assessment, highlighting its potential to improve clinical trial outcomes. AI techniques analyze vast datasets to predict adverse events, treatment responses, and operational risks. Despite high performance in studies, challenges such as data bias and limited generalizability remain. Addressing these issues can enhance drug development efficiency and patient safety. AI is poised to play a crucial role in future pharmacovigilance and personalized medicine.

INTRODUCTION

The development of new pharmaceuticals is a complex, costly, and time-consuming process. Traditional methods rely heavily on extensive clinical trials, which are fraught with risks, high failure rates, and significant resource expenditure. Ensuring drug safety and efficacy remains paramount, necessitating innovative approaches to predict and mitigate potential risks early in the development pipeline.

Artificial intelligence (AI), encompassing machine learning (ML), deep learning (DL), and natural language processing (NLP), has emerged as a transformative tool to address these challenges. By analyzing vast and diverse datasets—including clinical trial data, electronic health records (EHRs), genomic information, and scientific literature—AI models can predict adverse drug reactions (ADRs), optimize trial design, and assess operational risks, thus accelerating development timelines and improving patient outcomes.

This review presents a comprehensive overview of AI's role in drug safety and efficacy evaluation, focusing on recent research trends, methodologies, data sources, assessment metrics, limitations, and future directions.

Clinical trials are critical for drug approval but have a failure rate of nearly 90%, mainly due to safety issues, lack of efficacy, or operational challenges. These failures cost billions and delay treatment availability. Artificial Intelligence is now being applied to predict and mitigate clinical trial risks before trials begin or during execution. This review summarizes AI applications in safety, efficacy, and operational risk assessment from January 2013 to July 2024. The objective is to understand how AI models are built, what data they use, how well they perform, and what limitations exist. AI-based risk assessment aims to improve decision-making, reduce failures, and support risk-based monitoring frameworks in drug development.

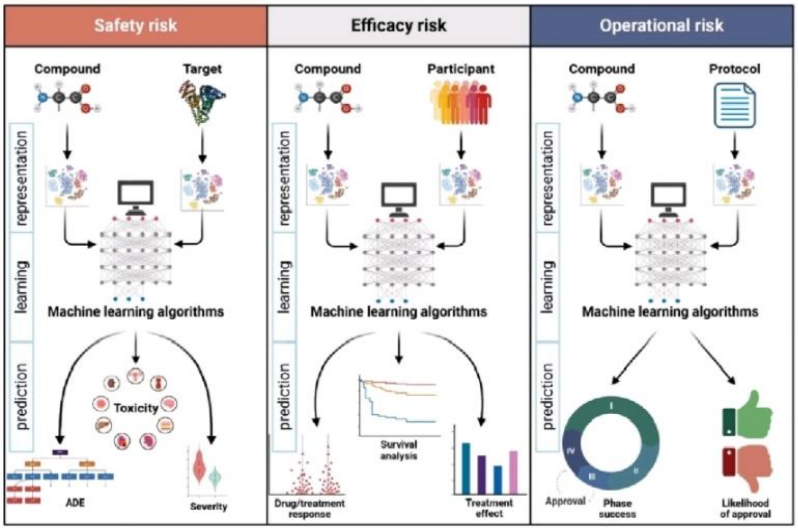
Risk Categories in Clinical Trials

AI studies in this domain are grouped into three major risk types:

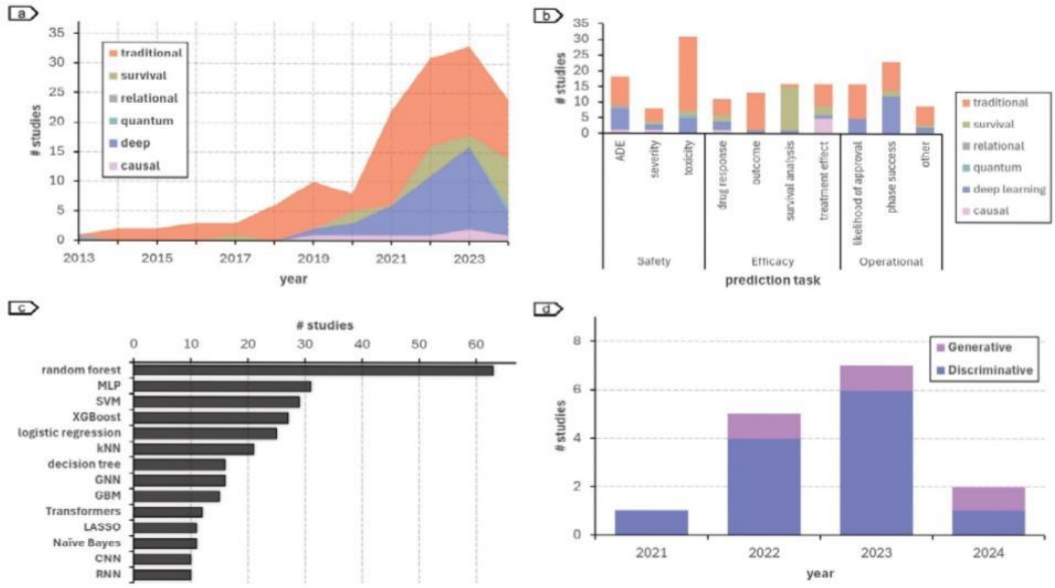
1. Safety Risk: Predicts adverse drug events, toxicity, drug-induced liver/kidney injury, and mortality. Models use chemical structure, molecular properties, or patient data to flag compounds likely to cause harm. Example: Predicting if a new molecule will cause serious ADEs using SIDER database.

2. Efficacy Risk: Determines whether a drug will work for a given condition or patient. Includes drug response prediction, treatment outcome classification, treatment effect estimation, and progression-free survival. Example: Using patient symptom profiles to predict antidepressant response.

3. Operational Risk: Focuses on trial execution. Predicts phase transition success, regulatory approval, protocol design flaws, recruitment/enrollment issues, and trial discontinuation. Example: Predicting if a Phase II trial will succeed and move to Phase III.



Trend of AI Risk Prediction for Clinical trial



Machine Learning Model used in Risk Assessment of Clinical Trial

Most studies address only one risk type. Only one reviewed study combined safety and efficacy prediction, showing a major research gap in integrated risk modeling.

Data Sources and Evaluation Metrics

Data availability differs by risk type and impacts model reliability:

- **Safety Studies:** Mostly use public benchmarks. SIDER is the main source, containing adverse drug reactions extracted from FDA FAERS. Median dataset: 1,341 compounds. 18 studies used only public data.

- **Efficacy Studies:** Rely heavily on private datasets. Most use data from individual clinical trials. Median per study: 1 trial and 1,250 participants. 29 studies used at least one private dataset.
- **Operational Studies:** Use public data from ClinicalTrials.gov. Median: 75,174 protocols.
- **Common metrics:** AUROC was used in 94 studies, accuracy in 56, and recall in 51. For regression tasks, RMSE was the only top-10 metric. Safety and operational studies report a median of 3 metrics per study, while efficacy studies report 2, suggesting less comprehensive evaluation.
- **AUROC (Area Under ROC Curve):** Measures discriminative ability. Accuracy, Precision, Recall, F1-score: Standard classification metrics.
- **Matthews Correlation Coefficient (MCC):** Handles imbalanced datasets.
- **RMSE (Root Mean Square Error):** Used for regression tasks like dose-response prediction.

  Current Trends and Findings

AI Model Performance

Direct comparison is hard due to different tasks and datasets. For AUROC:

- **Safety/ADE Prediction:** Highest performance by Masum Shah et al. at 96.6% AUROC. Zhao et al. 93.1%, Galeano et al. and Zhong et al. 92.0%. All top 3 studies >90% AUROC.
- **Efficacy/Outcome Prediction**: Top models by Lei et al. 87.4%, followed by others between 84.0%–87.0%.
- **Operational/Phase Success:** Ferdowsi et al. studies ranked top 3, with AUROC 92.3%–92.7%.

Dataset size varies: Operational models train on $\sim 10^5$ protocols, while safety models use $\sim 10^3$ compounds and efficacy models use $\sim 10^2$ participants. Larger datasets in operational risk may explain higher performance.

AI Methodologies and Trends

Multiple AI approaches are applied:

- **Machine Learning (ML) Approaches:** Traditional ML algorithms dominate current risk prediction models due to their interpretability and robustness. Algorithms like random forests, support vector machines (SVM), gradient boosting machines (GBM), and

XGBoost are extensively used to analyze structured data, such as clinical trial results, genomic data, and adverse event reports**.**

- **Deep Learning (DL) Techniques :** DL models, including neural networks, convolutional neural networks (CNN), graph neural networks (GNN), transformers, and recurrent neural networks (RNN), excel at handling unstructured data like free-text clinical notes, molecular structures, and images. These models automatically extract features, improving prediction accuracy for complex risk patterns.
- **Causal and Relational Learning:** Emerging approaches focus on causal inference to identify cause-effect relationships between variables, enhancing the understanding of factors influencing drug responses. Relational learning models handle complex relationships in biological networks and drug interactions.
- **Large Language Models (LLMs):** Recent developments incorporate LLMs, such as BERT and GPT, for textual data representation and risk prediction from protocols, scientific literature, and reports. These models can encode semantic information, enabling nuanced understanding of clinical trial documents.
- **Generative AI**: Still minimal in clinical trial risk prediction.
- **Key trend:** Multi-task learning is emerging to jointly predict safety, efficacy, and operational risks. This improves data efficiency and leverages shared representations. Yazdani et al. used multi-task learning for ADE entity normalization. Tan used it for anti-cancer drug response.

Efficacy Prediction Case Studies

Efficacy failures cause most Phase II/III terminations. AI applications include:

- **Drug Response:** Wang et al. 2023 developed XMR, an explainable multimodal network integrating molecular, genomic, and clinical data.
- **Treatment Outcome:** Chekroud et al. 2017 used symptom clustering to re-evaluate antidepressant efficacy. Faraone et al. 2021 and 2022 showed early ADHD symptom changes predict viloxazine efficacy using ML.
- **Disease-Specific Models:** Ezzati & Lipton 2020 for Alzheimer's trials, Beacher et al. 2021 for prostate cancer Phase III outcomes, Gottlieb et al. 2021 for secukinumab in psoriatic arthritis.
- **Vaccine Efficacy:** Dorigatti et al. 2018 used ML to refine efficacy estimates for Sanofi Pasteur's dengue vaccine CYD-TDV.

Limitations of Current AI Methods

Despite high AUROC, real-world use is limited by:

1. Selection Bias: Safety datasets cover ~10^3 compounds vs. ~10^{60} drug-like space or ~10^8 in PubChem. Efficacy studies often use 1 trial, so generalizability to new drugs/conditions is unknown.

2. Evaluation Weakness: Many studies ignore imbalanced data. Robust metrics like F1-score, MCC, and weighted accuracy are underused. Lack of external validation.

3. Retrospective Design: No prospective studies or real-time data integration. Causality cannot be established.

4. Phase Ignorance: Safety models are non-phase-specific but ADEs depend on dose/population which vary by phase. Efficacy models focus on Phase III, but Phase II failures create survivorship bias.

Impact of Clinical Trial Phase

Trial phase affects risk but is often overlooked:

- **Operational Risk:** 27 studies covered ≥3 phases, improving generalizability vs. safety/efficacy studies that focus on single phases.
- **Efficacy Risk:** Most models use Phase III data only. But efficacy is first tested in Phase II. Drugs failing Phase II never reach Phase III, so models are biased toward successful compounds. Lu et al. 2022 is a notable Phase I-III model for PK/PD prediction.
- **Safety Risk:** All safety studies are non-phase-specific. However, population and dosage differ by phase, impacting ADE risk. Phase I application: Bedon et al. proposed ML to predict maximum tolerated dosage to avoid exposing participants to toxic levels.

Recommendations for Future Research

To improve clinical utility:

1. Data Improvements: Add dosage, route of administration, and demographics to safety models. Use larger intervention-outcome scenarios.

2. Better Evaluation: Consistently use F1-score, MCC, weighted accuracy. Validate on different drugs, conditions, and populations.

3. Prospective Studies: Move beyond retrospective analysis. Use real-time safety, efficacy, and operational data during trials to establish causality.

4. Integrated Models: Develop multi-task AI that simultaneously predicts safety, efficacy, and operational risks. This captures interdependencies and supports holistic risk-based monitoring. Example: Jointly predicting toxicity and efficacy for a dose-selection model.

5. Regulatory Acceptance and Ethical Considerations: Engaging regulatory agencies early in the development process and ensuring transparency and explainability of AI models will facilitate acceptance and ethical deployment.

CONCLUSION

Artificial Intelligence (AI) is revolutionizing the landscape of drug safety and efficacy assessment by enabling faster, more accurate, and data-driven decision-making throughout the drug development lifecycle. From predicting adverse drug reactions to optimizing clinical trial designs and enhancing pharmacovigilance systems, AI offers powerful tools that augment human expertise and improve patient outcomes. Despite its transformative potential, challenges such as data privacy, algorithmic bias, regulatory acceptance, and the need for robust validation must be addressed to ensure responsible integration. As AI technologies continue to evolve, their strategic implementation will be critical in creating safer, more effective therapies and accelerating the path from discovery to delivery.

KEY REFERENCES:

1. Sové et al. 2022. _J. Immunother. Cancer_ 10. Virtual clinical trials of anti-PD-1/anti-CTLA-4 in HCC.
2. Wang et al. 2023. _Front. Bioinforma. 3. XMR: explainable multimodal neural network.
3. Chekroud et al. 2017. _JAMA Psychiatry_ 74:370–378. Antidepressant efficacy via symptom clustering.
4. Dorigatti et al. 2018. _Nat. Commun. 9:3644. ML for dengue vaccine efficacy.
5. Faraone et al. 2021. _Psychiatry Res._ 296:113664. ML for viloxazine in ADHD.
6. Faraone et al. 2022. _Psychiatry Res._ 318:114922. Early change predicts viloxazine efficacy.
7. Ezzati & Lipton 2020. _J. Alzheimers Dis._ 74:55–63. ML improves Alzheimer's trial efficacy.
8. Beacher et al. 2021. _Algorithms_ 14. ML predicts Phase III prostate cancer outcomes.
9. Dorsey, E. R., Venuto, C., Venkataraman, V., Harris, D. A. & Kieburtz, K. Novel Methods and Technologies for 21st-Century Clinical Trials: A Review. JAMA Neurol. 72, 582–588 (2015).

10. Downing, N. S., Aminawung, J. A., Shah, N. D., Krumholz, H. M. & Ross, J. S. Clinical Trial Evidence Supporting FDA Approval of Novel Therapeutic Agents, 2005-2012. JAMA 311, 368–377 (2014).
11. Schlander, M., Hernandez-Villafuerte, K., Cheng, C.-Y., Mestre-Ferrandiz, J. & Baumann, M. How Much Does It Cost to Research and Develop a New Drug? A Systematic Review and Assessment. PharmacoEconomics 39, 1243–1269 (2021).
12. DiMasi, J. A., Feldman, L., Seckler, A. & Wilson, A. Trends in Risks Associated With New Drug Development: Success Rates for Investigational Drugs. Clin. Pharmacol. Ther. 87, 272–277 (2010).
13. Mentz, R. J. et al. Good Clinical Practice Guidance and Pragmatic Clinical Trials. Circulation 133, 872–880 (2016).
14. Barnes, B. et al. Risk-Based Monitoring in Clinical Trials: Past, Present, and Future. Ther. Innov. Regul. Sci. 55, 899 (2021).
15. Agrafiotis, D. K. et al. Risk-based Monitoring of Clinical Trials: An Integrative Approach. Clin. Ther. 40, 1204–1212 (2018).
16. Selker, H. P. et al. Efficacy and Effectiveness Too Trials: Clinical Trial Designs to Generate Evidence on Efficacy and on Effectiveness in Wide Practice. Clin. Pharmacol. Ther. 105, 857–866 (2019).
17. Simović, M. & Nikolić, N. Challenges of risk-based monitoring of clinical trials. Clin. Res. Regul. Aff. 32, 83– 87 (2015).
18. Fneish, F., Schaarschmidt, F. & Fortwengel, G. Improving Risk Assessment in Clinical Trials: Toward a Systematic Risk-Based Monitoring Approach. Curr. Ther. Res. 95, 100643 (2021).
19. Newman, P. A., Guta, A. & Black, T. Ethical Considerations for Qualitative Research Methods During the COVID-19 Pandemic and Other Emergency Situations: Navigating the Virtual Field. Int. J. Qual. Methods 20, 16094069211047823 (2021).
20. Yao, B., Zhu, L., Jiang, Q. & Xia, H. A. Safety Monitoring in Clinical Trials. Pharmaceutics 5, 94–106 (2013)
21. Harrer, S., Shah, P., Antony, B. & Hu, J. Artificial Intelligence for Clinical Trial Design. Trends Pharmacol. Sci. 40, 577–591 (2019).
22. Badwan, B. A. et al. Machine learning approaches to predict drug efficacy and Toxicity in oncology. Cell Rep. Methods 3, 100413 (2023).

23. Feijoo, F., Palopoli, M., Bernstein, J., Siddiqui, S. & Albright, T. E. Key Indicators of phase transition for clinical trials through machine learning. Drug Discov. Today 25, 414–421 (2020).
24. Alowais, S. A. et al. Revolutionizing healthcare: the role of artificial intelligence In clinical practice. BMC Med. Educ. 23, 689 (2023).
25. Moingeon, P., Kuenemann, M. & Guedj, M. Artificial intelligence-enhanced drug Design and development: Toward a computational precision medicine. Drug Discov. Today 27, 215–222 (2022).
26. Ngayua, E. N., He, J. & Agyei-Boahene, K. Applying advanced technologies to Improve clinical trials: a systematic mapping study. Scientometrics 126, 1217–1238 (2021).
27. Askin, S., Burkhalter, D., Calado, G. & El Dakrouni, S. Artificial Intelligence Applied to clinical trials: opportunities and challenges. Health Technol. 13, 203—213 (2023).
28. Weissler, E. H. et al. The role of machine learning in clinical research: Transforming the future of evidence generation. Trials 22, (2021).
29. Zame, W. R. et al. Machine learning for clinical trials in the era of COVID-19. Stat. Biopharm. Res. 12, 506– 517 (2020).
30. Paul, D. et al. Artificial intelligence in drug discovery and development. Drug Discov. Today 26, 80–93 (2020)