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Petković, Karlo; Strika, Zdeslav; Likić, Robert; Lucijanić, Marko

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COMMENTARY

Spotlight commentary: Integrating artificial intelligence in clinical pharmacology: Opportunities, challenges and ethical imperatives

Karlo Petkovic[1] | Zdeslav Strika[1] | Robert Likic[1,2] | Marko Lucijanic[1,3,4]

[1]School of Medicine, University of Zagreb, Zagreb, Croatia

[2]Department of Internal Medicine, Unit for Clinical Pharmacology, Clinical Hospital Centre Zagreb, Zagreb, Croatia

[3]Department of Internal Medicine, Unit for Hematology, University Hospital Dubrava, Zagreb, Croatia

[4]Department of Scientific Research and Translational Medicine, University Hospital Dubrava, Zagreb, Croatia

Correspondence
Robert Likic, Department of Internal Medicine, Unit for Clinical Pharmacology, Clinical Hospital Centre Zagreb, Zagreb, Croatia.
Email: robert.likic@mef.hr

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1 | INTRODUCTION

The integration of artificial intelligence (AI) into clinical pharmacology heralds a transformative era in healthcare, promising greater efficiencies in drug discovery, personalized medicine and patient care. AI, defined as the simulation of human intelligence by machines, encompasses various subsets including machine learning (ML) and deep learning (DL). ML involves algorithms that enable computers to learn from and make predictions based on data, while DL, a subset of ML, utilizes neural networks with many layers to analyse complex datasets. AI's capacity to process vast datasets exceeds that of the conventional methodologies, providing new insights into drug efficacy and patient outcomes. These large datasets are crucial for work with AI algorithms and include types of data analysis particularly relevant for pharmacology such as natural language processing (NLP), large language models (LLMs), voice recognition, numerical data, multi-omic data integration and image processing. This spotlight commentary explores the multifaceted roles of AI in clinical pharmacology (Figure 1), addressing its potential in accelerating drug discovery, optimizing clinical trials and navigating the ethical landscape associated with its adoption by highlighting a few relevant recent publications on the topic.

We start the overview with the paper by Saikin et al. (2019)[1] who advocated integration of AI and ML tools into a unified, closed-loop discovery platform. This approach may be crucial for transforming early-stage drug development, where the ability to rapidly test hypotheses and iterate findings can significantly shorten the time to discovery. Closed-loop systems utilize AI not only to design experiments and predict outcomes but also to automatically adjust the experimental parameters based on real-time data. This results in a highly efficient cycle of hypothesis generation, testing and learning which is much faster than traditional drug discovery methods. By integrating diverse AI tools—from predictive analytics to robotic process automation—these platforms could handle complex datasets and experimental conditions, improving the accuracy and speed of identifying viable drug candidates.

Furthermore, Lou and Wu (2021)[2] focused on the application of AI in identifying new drug-target pairs, particularly for diseases with well-understood mechanisms and drugs exhibiting medium chemical novelty. The use of AI in this context would allow for the exploration of vast chemical spaces and biological interactions more comprehensively and rapidly than human capabilities allow. AI algorithms analyse existing data to predict how new compounds would interact with specific targets, which is crucial for the development of targeted therapies. By leveraging pattern recognition and ML, AI tools can uncover nonobvious relationships between compounds and biological targets, thereby opening up new avenues for therapy that might not have been discovered through conventional research methods. This approach could be very helpful in drug repurposing, where AI identifies novel therapeutic uses for existing drugs, potentially accelerating the drug development process and reducing costs.

While the repurposing of antiviral and anti-inflammatory drugs for COVID-19 did not yield successful outcomes despite extensive data and AI efforts, recent advancements in AI have significantly impacted drug discovery and development. Zakeri (2024)[3] highlighted how AI-assisted experiments in adeno-associated virus gene therapy research have identified novel pathways and mechanisms, paving the way for new therapeutic approaches. Similarly, Verma et al. (2024)[4]

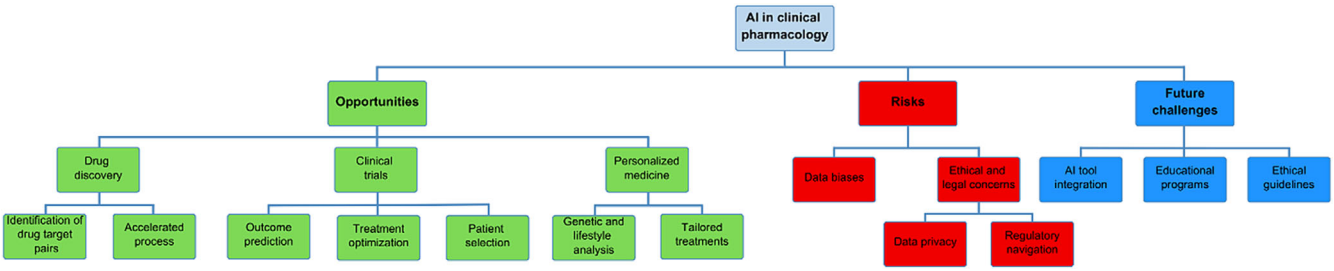

FIGURE 1 Artificial intelligence (AI) in clinical pharmacology: opportunities, risks and future challenges.

demonstrated the potential of AI in drug repositioning, where existing drugs are repurposed for new therapeutic uses by uncovering novel targets and mechanisms of action. Satpathy (2024)[5] further emphasized the role of advanced AI algorithms in drug design and development, showcasing their effectiveness in classifying and screening of compounds. This has led to the discovery of new drug candidates with higher success rates in preclinical trials. Moreover, Vairamani et al. (2024)[6] discussed the application of AI-driven predictive models in CNS drug discovery, which have enhanced the efficiency of the process by accurately predicting drug efficacy and safety profiles, thereby reducing clinical trial failures.

AI is revolutionizing clinical trial design by identifying subjects most likely to respond to treatments and using targeted biomarkers to reduce trial sizes, significantly lowering Phase III study costs as reported by Askin et al. (2023).[7] AI analyses extensive datasets to predict positive responders and develop biomarkers for patient stratification, enhancing trial efficiency. However, this targeted approach might limit result generalizability, as traditional large-scale trials provide broader demographic insights into drug efficacy and safety. To mitigate these concerns, AI could integrate diverse data sources, simulate outcomes for varied populations and function as a continuous learning system that evolves with new data. Incorporating diverse data ensures demographic representation, while simulations could offer insights into broader applicability. Continuous learning would keep AI models accurate and relevant. Additionally, ethical and regulatory frameworks would be essential to ensure AI-driven trials are efficient, cost-effective and ethically sound. By addressing generalizability issues and maintaining rigorous standards, AI holds promise for improving clinical trial precision, reducing costs and ultimately enhancing patient outcomes and drug development efficiency.

Vora et al. (2023)[8] in their recent article provided a detailed analysis of how AI is revolutionizing pharmaceutical technologies and drug delivery systems. Their research highlights AI's role in designing drug formulations that optimize the therapeutic impact while minimizing side effects. One key application is the development of nano-drug delivery systems, where AI models simulate how nanoparticles interact with different types of cells and tissues. These models help in designing nanoparticles that can precisely target diseased cells, thereby increasing the efficacy and safety of treatments. Additionally, AI is used to optimize the manufacturing processes of these formulations, ensuring that they are produced with high precision and consistency. By integrating AI into both the design and production stages, pharmaceutical companies can achieve higher levels of customization and scalability in their product offerings.

AI could also play a pivotal role in refining clinical trials, particularly in the optimization of study designs and enhancement of data analysis capabilities. In their recent BJCP article, Ryan et al. (2024)[9] highlighted how AI algorithms would be capable of simulating clinical trial outcomes based on historical data, which could predict the efficacy and safety profiles of new drugs before actual clinical testing. This predictive capability could significantly reduce the risk and costs associated with clinical trials by identifying potential failures early in the drug development process. Furthermore, AI-driven tools are being developed to monitor patient compliance and adverse events in real-time during clinical trials, ensuring that any significant issues can be addressed promptly to maintain the integrity and validity of the trial results.

Furthermore, AI has the potential to revolutionize the management of approved medicines through several key avenues. Firstly, AI could optimize prescribing by analysing electronic health records to tailor medication plans to individual patient needs, thereby enhancing treatment efficacy and reducing adverse reactions as suggested by Khan et al. (2023).[10] In managing polypharmacy, AI systems could rationalize medication regimens by identifying and mitigating drug–drug and drug–food interactions, as well as assessing risks associated with multiple medications as suggested by O'Reilly et al. (2023).[11] Additionally, AI would enhance pharmacovigilance by leveraging data from electronic health records, social media and other sources to detect and analyse adverse drug reactions in real-time as reported by Chalasani et al. (2023).[12] This capability would allow for more rapid and precise monitoring of drug safety, ultimately improving patient outcomes and ensuring safer prescribing practices. For instance, AI solutions can increase medication adherence in patients with noncommunicable diseases by organizing and mining data from unstructured electronic medical records as reported by Babel et al. (2021).[13] Furthermore, Blasiak et al. (2020) show that the development of AI tools like CURATE.AI showcases how personalized medicine can be optimized by identifying patient-specific care strategies through health data analytics.[14] The integration of AI into medication management represents a significant advancement toward more personalized and efficient healthcare.

By contrast, Terranova and Venkatakrishnan (2024)[15] explored the transformative potential of ML in oncology, particularly in modelling disease trajectories and predicting treatment outcomes. Their research emphasized the use of high-dimensional biomarker data, such as circulating tumour DNA and radiomics profiles, which are critical for understanding the complex dynamics of cancer progression. By employing ML algorithms, clinicians could predict survival outcomes with greater accuracy, personalize treatment plans and monitor the effectiveness of interventions in real-time. Their model's informed precision medicine approach was pivotal not only in enhancing the efficacy of treatments but also in minimizing unnecessary side effects by accurately predicting which patients were most likely to benefit from specific therapies. The integration of ML in these processes represents a major leap toward more dynamic and responsive cancer care, where decisions can be continually adjusted based on real-time data analysis, providing hope of significantly improving patient outcomes.

Despite its vast potential, the integration of AI into healthcare systems is fraught with challenges that must be carefully managed. Kelly et al. (2019)[16] outlined several key hurdles, including the translation of AI applications into clinical practice, ensuring patient safety and navigating complex regulatory landscapes. These challenges are compounded by AI systems' "black box" nature, where decision-making processes are not always transparent, making clinical validation particularly difficult.

Moreover, AI's reliance on extensive data sets introduces risks of algorithmic bias and data privacy concerns. These issues necessitate robust clinical evaluations and the development of intuitive metrics that focus not only on technical accuracy but also on quality of care and patient outcomes. As Bužančić et al. (2024)[17] noted, while AI can support clinical reasoning and decisions, its limitations, including ambiguities and inaccuracies, underscore its role as a supplementary tool rather than a standalone decision-maker.

In terms of ethics, Belenguer (2022)[18] highlights how it remains crucial to consider the potential for AI bias, as the output of AI systems heavily relies on input, which can inherently carry biases. The robust debate surrounding this issue varies significantly depending on whether one's perspective is philosophical or technical. Philosophical approaches might emphasize the ethical implications and moral responsibilities, while technical perspectives focus on mitigating bias through improved algorithms and data management practices. Addressing AI bias necessitates a multidisciplinary effort to ensure ethical and unbiased AI applications across different fields.

The implementation of AI in clinical pharmacology raises significant ethical concerns, particularly the potential for its misuse in the synthesis of bioweapons and toxins, as highlighted by Rubinic et al. (2024).[19] AI's ability to process complex biological data not only accelerates drug discovery but also poses risks if repurposed for creating harmful biological agents. This dual-use nature of AI technologies underscores the necessity for stringent ethical standards and robust legal frameworks specifically tailored to oversee AI's application in sensitive areas. Ethical standards for AI should mandate transparency, accountability and secure access to prevent misuse and need regular updates to keep pace with technological advancements. Education on these topics is also of high importance as highlighted by Watari and Tokuda (2023).[20] Additionally, robust legal frameworks remain essential to enforce these ethical standards, with strict penalties for violations and provisions to align AI use with health regulations and international standards. These laws should also facilitate international cooperation to manage the global implications of AI misuse effectively. Addressing these issues requires a collaborative approach involving ethicists, legislators, scientists and industry leaders. Such collaboration would be crucial for developing comprehensive strategies that balance the benefits of AI with potential risks, ensuring AI's potential is harnessed responsibly and safely in clinical pharmacology. This collaborative effort would help in establishing an environment where technological advancements contribute positively without compromising ethical standards or public safety.

Moreover, it is essential to recognize that advanced statistical algorithms, such as Bayesian methods, nonlinear mixed effects modelling and quantitative systems pharmacology, have long been established as powerful tools for design, analysis and interpretation in clinical pharmacology. These methodologies, underpinned by robust mechanism-based principles, have been shown to enhance efficacy and reduce attrition in drug development. Regulatory agencies and clinical pharmacologists in pharmaceutical research and development increasingly recommend these approaches, as evidenced by several guidelines that advocate their use.[21–23] In this context, AI can play a supportive role, particularly in automating some of the more time-consuming and computationally intensive steps involved in these advanced methodologies. However, it is imperative to distinguish between the roles of AI in early drug discovery—where its utility in hypothesis generation is clear—and the more nuanced processes of hypothesis testing and inferential reasoning. The current AI tools often lack the sophistication required for these complex inferential steps, leading to concerns about the mechanical application of AI without sufficient consideration of data quality, validation and interpretation. As the field advances, clinicians and researchers must remain vigilant in ensuring that AI is integrated thoughtfully, complementing rather than replacing the rigorous quantitative methods that have long been the cornerstone of clinical pharmacology.

Further complicating the ethical landscape is the need for adequate AI education within pharmacy and medical curricula. Busch et al. (2024)[24] reported that while students were generally positive about AI in medicine, those with prior AI coursework felt better prepared for its professional application. This underscores the importance of integrating AI education into healthcare training programmes to equip future professionals with the necessary skills and ethical understanding to use AI responsibly.

AI holds transformative potential for clinical pharmacology, offering significant advancements in drug discovery, clinical trials and personalized medicine.[25,26] However, realizing this potential requires overcoming substantial challenges, including ethical issues, data biases and integration hurdles. One crucial strategy for effective implementation involves integrating all AI tools and technologies into a single platform, which could streamline processes, decrease redundancies

and enhance data interoperability. Such consolidation would be essential for harnessing the full capabilities of AI, allowing for more cohesive and efficient advancements in drug development. Future directions should focus on developing educational programmes that address these integration needs and establishing guidelines that ensure AI's ethical and effective implementation in healthcare settings. As we move forward, it is crucial to continue evaluating AI's impact on patient outcomes and to adapt our approaches based on these insights. Collaboration between technologists, clinicians and ethicists will be crucial in harnessing AI's full potential while safeguarding against its risks.

AUTHOR CONTRIBUTIONS

All authors contributed equally to drafting of the manuscript and agreed with the final version that was submitted to the journal.

CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this spotlight commentary are derived from publicly available references, as cited within the manuscript. No new datasets were generated or analyzed during the preparation of this commentary. For further information or inquiries, please contact the corresponding author.

ORCID

Robert Likic https://orcid.org/0000-0003-1413-4862
Marko Lucijanic https://orcid.org/0000-0002-1372-2040

REFERENCES

1. Saikin SK, Kreisbeck C, Sheberla D, Becker JS, A AG. Closed-loop discovery platform integration is needed for artificial intelligence to make an impact in drug discovery. *Expert Opin Drug Discovery*. 2019;14(1):1-4. doi:10.1080/17460441.2019.1546690
2. Lou B, Wu L. AI on drugs: can artificial intelligence accelerate drug development? Evidence from a large-scale examination of bio-pharma firms. In: *MISQ Forthcoming*; 2021.
3. AAV gene therapy research with AI-assisted biological experiments|-form bio [internet]. [cited 2024 Aug 9]. Available from: https://www.formbio.com/blog/ai-assisted-aav-research
4. Verma S, Nainwal N, Singh A, Kukreti G, Dobhal K. An overview of computational-based strategies for drug repositioning. In: *Integrating Metaheuristics in Computer Vision for Real-World Optimization Problems*; 2024:81-97. doi:10.1002/9781394230952.ch5
5. Satpathy R. Artificial intelligence techniques in the classification and screening of compounds in computer-aided drug design (CADD) process. In: *Artificial Intelligence and Machine Learning in Drug Design and Development*; 2024:473-497. doi:10.1002/9781394234196.ch15
6. Vairamani AD, Adhikary S, Banerjee K. Data processing method for AI-driven predictive models for CNS drug discovery. In: *Artificial Intelligence and Machine Learning in Drug Design and Development*; 2024:223-249. doi:10.1002/9781394234196.ch8
7. Askin S, Burkhalter D, Calado G, El Dakrouni S. Artificial intelligence applied to clinical trials: opportunities and challenges. *Health Technol (Berl)*. 2023;13(2):203-213. doi:10.1007/s12553-023-00738-2
8. Vora LK, Gholap AD, Jetha K, Thakur RRS, Solanki HK, Chavda VP. Artificial intelligence in pharmaceutical technology and drug delivery design. *Pharmaceutics*. 2023;15(7):15. doi:10.3390/pharmaceutics15071916
9. Ryan DK, Maclean RH, Balston A, Scourfield A, Shah AD, Ross J. Artificial intelligence and machine learning for clinical pharmacology. *Br J Clin Pharmacol*. 2024;90(3):629-639. doi:10.1111/bcp.15930
10. Khan O, Parvez M, Kumari P, Parvez S, Ahmad S. The future of pharmacy: how AI is revolutionizing the industry. *Intelligent Pharmacy*. 2023;1(1):32-40. doi:10.1016/j.ipha.2023.04.008
11. O'Reilly D, McGrath J, Martin-Loeches I. Optimizing artificial intelligence in sepsis management: opportunities in the present and looking closely to the future. *Journal of Intensive Medicine*. 2024;4(1):34-45. doi:10.1016/j.jointm.2023.10.001
12. Chalasani SH, Syed J, Ramesh M, Patil V, Pramod Kumar TM. Artificial intelligence in the field of pharmacy practice: a literature review. *Explor Res Clin Soc Pharm*. 2023;12:100346. doi:10.1016/j.rcsop.2023.100346
13. Babel A, Taneja R, Mondello Malvestiti F, Monaco A, Donde S. Artificial intelligence solutions to increase medication adherence in patients with non-communicable diseases. *Front Digit Health*. 2021;3:669869. doi:10.3389/fdgth.2021.669869
14. Blasiak A, Khong J, Kee T. CURATE.AI: optimizing personalized medicine with artificial intelligence. *SLAS Technol*. 2020;25(2):95-105. doi:10.1177/2472630319890316
15. Terranova N, Venkatakrishnan K. Machine learning in modeling disease trajectory and treatment outcomes: an emerging enabler for model-informed precision medicine. *Clin Pharmacol Ther*. 2024;115(4):720-726. doi:10.1002/cpt.3153
16. Kelly CJ, Karthikesalingam A, Suleyman M, Corrado G, King D. Key challenges for delivering clinical impact with artificial intelligence. *BMC Med*. 2019;17(1):195. doi:10.1186/s12916-019-1426-2
17. Bužančić I, Belec D, Držaić M, et al. Clinical decision-making in benzodiazepine deprescribing by healthcare providers vs. AI-assisted approach. *Br J Clin Pharmacol*. 2024;90(3):662-674. doi:10.1111/bcp.15963
18. Belenguer L. AI bias: exploring discriminatory algorithmic decision-making models and the application of possible machine-centric solutions adapted from the pharmaceutical industry. *AI and Ethics*. 2022;2(4):771-787. doi:10.1007/s43681-022-00138-8
19. Rubinic I, Kurtov M, Rubinic I, Likic R, Dargan PI, Wood DM. Artificial intelligence in clinical pharmacology: a case study and scoping review of large language models and bioweapon potential. *Br J Clin Pharmacol*. 2024;90(3):620-628. doi:10.1111/bcp.15899
20. Watari T, Tokuda Y. Letter to the editor concerning the article: "artificial intelligence in clinical pharmacology: a case study and scoping review of large language models and bioweapon potential". *Br J Clin Pharmacol*. 2023;89(12):3771-3772. doi:10.1111/bcp.15922
21. Wang H, Arulraj T, Anbari S, Popel AS. Quantitative systems pharmacology modeling of macrophage-targeted therapy combined with PD-L1 inhibition in advanced NSCLC. *Clin Transl Sci*. 2024;17(6):e13811. doi:10.1111/cts.13811
22. D'Agate S, Chavan C, Manyak M, et al. Model-based meta-analysis of the time to first acute urinary retention or benign prostatic hyperplasia-related surgery in patients with moderate or severe symptoms. *Br J Clin Pharmacol*. 2021;87(7):2777-2789. doi:10.1111/bcp.14682
23. Schuirmann DJ, Grosser S, Chattopadhyay S, Chow SC. On Bayesian analysis and hypothesis testing in the determination of bioequivalence. *Clin Pharmacol Ther*. 2019;105(2):304-306. doi:10.1002/cpt.1291
24. Busch F, Hoffmann L, Truhn D, et al. International pharmacy students' perceptions towards artificial intelligence in medicine—a

multinational, multicentre cross-sectional study. *Br J Clin Pharmacol*. 2024;90(3):649-661. doi:10.1111/bcp.15911

25. Lucijanic M, Likic R. The future is now, old man. *Br J Clin Pharmacol*. 2024;90(3):618-619. doi:10.1111/bcp.16011
26. Gawade VR, Apar KS, Mapari RD, Lahane HS, Pawar DVR. From data to drugs a review: harnessing AI for accelerated pharmaceutical development. *Int Adv Res Sci Commun Technol*. 2023;3:346-350. doi: 10.48175/IJARSCT-12456

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