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Role of Artificial Intelligence (AI) and Machine Learning (ML) in Pharmaco-epidemiology: A Narrative Review

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Abstract

A crucial area of study called pharmaco-epidemiology combines pharmacology and epidemiology to investigate how pharmaceuticals are used, work, and if they are safe in a huge population. Clinical studies, pre-clinical trials, and medication research and development are just a few of the pharmaco-epidemiology research areas that could benefit from the application of artificial intelligence (AI) and machine learning (ML). Huge volumes of patient's data can be analyzed using AI and ML to pinpoint patient's subpopulations that are more likely to benefit from specific pharmaceutical treatments. Researchers have the ability to develop more tailored treatment plans that improve patient's outcomes by supplying this insight. Additionally, AI and ML can assist in hastening the discovery of new drugs and reducing development costs by helping to identify a potential responder early on in the clinical trial process. Pre-clinical studies using AI and ML can be more productive, less expensive, and less time consuming to create, all of which can increase the likelihood of medication approval. These methods are also useful in the initial screening of pharmacological compounds and the biological success rate prediction stages of early drug research. Overall, AI and ML are crucial to many aspects of pharmaco-epidemiology clinical research and medication development, enhancing safety in clinical research by enabling the detection of safety hazards and adverse reactions, while also improving patient's outcomes and offering more individualized treatment plans.

Keywords: Artificial Intelligence; Machine Learning; Pharmaco-epidemiology; pharmaceutical; clinical trial.

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1. Introduction

Pharmaco-epidemiology is an interdisciplinary field that combines the principles of pharmacology and epidemiology to investigate the utilization, outcomes, and safety of medications in large populations. This field plays a critical role in understanding how drugs are used, their effectiveness, and the potential risks associated with their use. By identifying patterns and trends in drug utilization, researchers can gain insight into how drugs are utilized in real-world settings and identify areas where improvements can be made [1]. One of the primary objectives of pharmaco-epidemiology research is to educate medical professionals on the efficacy and safety of drugs [2]. By providing information on the effectiveness and potential risks associated with different drug therapies, healthcare providers can make informed decisions when selecting the most appropriate treatment options for patients. This in turn, can lead to improve patient's outcomes and better overall public health. The possibility of adverse drug reactions (ADEs) emphasizes the critical significance of pharmaco-epidemiology studies. ADEs can happen at any stage of the development and use of medicine and can range from minor side effects to potentially fatal situations [3]. By identifying and quantifying the risks associated with different drugs, researchers can help healthcare providers make informed decisions about the benefits and risks of different drug therapies [4]. This information can play an instrumental role in developing strategies to prevent ADEs from occurring in the first place. Pharmaco-epidemiology research is essential for identifying drug use and development limitations [5]. Researchers can help direct the development of new pharmaceuticals or the modification of existing therapies to better meet patient needs by detecting regions where new drugs are required or where existing drugs are not being utilized optimally [6]. In addition, pharmaco-epidemiology research can assist in identifying certain variables such as: Patient demographics, geographic location, and healthcare access that may affect drug consumption.

Artificial intelligence (AI) and machine learning (ML) have the potential to revolutionize the field of pharmaco-epidemiology by transforming the way we analyze massive electronic health records (EHRs) databases and claims data [7]. By leveraging these technologies, researchers can more effectively and correctly identify trends in drug usage, health conditions, and ADEs [8].

Artificial intelligence is a technology that enables machines to carry out operations like speech recognition, decision-making, and language translation that otherwise need human intelligence [9]. To collect and analyze data, identify patterns and trends, learn from them, and base predictions and choices on them, artificial intelligence requires algorithms. A branch of artificial intelligence called machine learning aims to make it possible for machines to learn from experience and advance without explicit programming [5]. To find patterns and relationships in data, machine learning algorithms utilize statistical

approaches and use this knowledge to make predictions or take action [10]. The machine becomes better and more effective at making predictions and judgments as it consumes more data.

Artificial intelligence and machine learning can be used to evaluate enormous amounts of healthcare data in the context of pharmaco-epidemiology research to spot trends, patterns, and potential hazards related to drugs [11]. With the help of these tools, it is feasible to examine electronic health records, insurance claims, and other data sources to find insights that are either impossible or very difficult to find using conventional research techniques [2]. Additionally, the use of artificial intelligence and machine learning can be used to create individualized patient treatment plans [12]. These technologies can examine patient data and offer tailored suggestions that take into consideration each patient's particular medical history, genetics, and other aspects [12]. As a result, there may be a reduction in the likelihood of negative medication reactions and better treatment outcomes. Artificial intelligence and machine learning can assist in the design of clinical trials to make them more successful and efficient [7]. Clinical trials can be more effectively targeted and conducted by using these technologies, which can evaluate patient's data to find subpopulations that may react differently to a treatment or medicine [13].

2. Subjects and Methods

The review comprehensively examined the various ways in which artificial intelligence and machine learning can be applied in the field of Pharmaco-epidemiology. It delves into different areas, such as the potential utilization of these technologies in clinical settings, pre-clinical trials, and drug research and development.

3. Results

3.1 Role of artificial intelligence & machine learning in Pharmaco-epidemiology in Clinical Studies

Machine learning & artificial intelligence are becoming increasingly popular in clinical research. By examining enormous amounts of patient's data including: Clinical and genetic data, these technologies can be used to pinpoint patient subpopulations that are more likely to respond to particular pharmaceutical therapies [14]. Researchers can create more individualized treatment regimens that improve patient's outcomes by finding biomarkers or other characteristics that predict a patient's propensity of reacting favorably to a certain treatment [15]. Finding patient populations most likely to benefit from a given drug is one of the most important advantages of artificial intelligence in clinical research. Artificial intelligence & machine learning can help to Identify possible responders early on in the clinical trial process and helps hasten the discovery of new drugs by cutting down on the time and costs needed for productive clinical research [16]. Furthermore, by foreseeing potential pharmacological side effects, artificial intelligence and machine learning can increase the safety of clinical research. These algorithms can examine patient's

data to find safety risks or adverse drug reactions that were previously undetected, perhaps saving lives by avoiding the omission of dangerous side effects [17]. For instance, researchers can apply artificial intelligence and machine learning to examine patient's genomic data to identify which patients are more likely to experience negative drug reactions [15]. This could aid in the early detection of potential safety risks by pharmaceutical companies, saving time and money during the medication development process. Additionally, by analyzing data from EHRs using artificial intelligence and machine learning, researchers can learn more about the behavior of patients and other variables that might influence how they respond to certain treatments [6]. These understandings can be used to develop more efficient, individually tailored treatment strategies, ultimately leading to better patient outcomes.

3.2 Pre-clinical trials

According to various statistics, the pre-clinical trials that include the process of creating a new drug are time-consuming, expensive, and have a low success rate. The average research and development (R&D) investment per drug is \$1.3 billion [18]. In addition, the median development times range from 5.9 to 7.2 years for non-oncology, 13.1 years for oncology, and only 13.8% of drug development programs result in approval [19]. Due to these difficulties, the drug development business is increasingly relying on machine learning approaches because of their automation, predictability, and anticipated rise in productivity [20]. From the perspective of both patients and businesses, increasing the efficiency of drug development is essential since it can decrease the costs, cut down on development time, and raise the probability of success (POS) [21].

For the past 15 to 20 years, machine learning techniques have been used in drug discovery with increasing sophistication. However, the most recent area where artificial intelligence and machine learning is anticipated to have a positive impact is in the planning, running, and analysis of clinical trials. Researchers can identify patient subpopulations that are more likely to respond to a specific medication as well as potential safety issues by utilizing machine learning algorithms to examine huge and complicated information. Clinical trials may become more effective and successful as a result, with quicker patient recruitment for the right patients and more precise evaluation of drug efficacy and safety [16]. Additionally, artificial intelligence and machine learning can improve clinical trial procedures, such as: choosing the best dosages, timing, and inclusion/exclusion standards and that's lead to more productive and successful trials. There is a rising need to gain insights from huge amounts of data generated from numerous sources in the fields of pre-clinical space. Biomedical literature and EMRs are examples of unstructured data that can be analyzed and understood using a technology called natural language processing (NLP) [22]. Researchers can find brand-new therapeutic targets and learn more about the

pathophysiology of diseases by using NLP from various sources [9]. Another method for facilitating drug development is predictive modeling. To find medication candidates with a higher chance of success, researchers anticipate protein structures and optimize the design of chemical compounds. The "Large p, Small n" problem, which occurs when there are more variables (p) than samples (n), can be solved using this strategy in some cases [23]. Machine learning techniques have been developed in recent years in response to the growing number of "big data" from genomics, imaging, and wearable technology [24]. In the post-marketing stage of drug development, where real-world data sources can be used to improve our understanding of a drug's benefit-risk profile, these techniques have shown to be extremely helpful [4]. As a result, it may be possible to identify patient subgroups that would benefit more from particular treatments than others, improving treatment sequence patterns, and enabling the practice of more individualized and precise medicine [17].

3.3 Application of Machine Learning & artificial intelligence in Research and Development

Machine learning is a valuable tool in various stages of early drug discovery, from the initial screening of drug compounds to predict a success rates based on biological factors. In addition, from the initial screening of pharmacological compounds to the prediction of success rates based on biological parameters, machine learning is an invaluable tool in the early phases of drug discovery [11]. Next-generation sequencing is a crucial tool in R&D and can benefit from machine learning to promote precision medicine by revealing pathophysiological causes and potential substitute treatment paths [25]. Despite that it's not able to predict outcomes like supervised learning and unsupervised learning is frequently used to spot patterns in data and is crucial to the study of pharmaceuticals [26].

By analyzing data from experimental and manufacturing processes, machine learning can also help pharmaceutical businesses to cut the time and cost associated with producing drugs. In situations where time is of the essence, machine learning can also be very helpful in finding new compounds or repurposing current medications to treat rare diseases or epidemics [11]. To address antibiotic resistance, a novel antibacterial medicine has already been successfully discovered using machine learning approaches. For instance, Halicin is a substance that can treat pan-drug-resistant *Acinetobacter Baumannii* infections and *Clostridium Difficile* infections in mouse models and it was recently discovered due to Artificial Intelligence [27]. Halicin was discovered more quickly and potentially for less money than standard procedures and it differs structurally from conventional antibiotics [28].

The use of machine learning and artificial intelligence in drug development have several benefits over conventional approaches. The ability to swiftly and effectively evaluate enormous datasets, which enables the identification of prospective therapeutic targets and compounds that would be impossible to

find through manual screening is a significant advantage [29]. Researchers can concentrate their efforts on the most promising ideas by using machine learning to estimate the success rate of therapeutic candidates based on biological characteristics like target specificity and pharmacokinetics. Furthermore, by identifying patient subgroups that are more likely to respond to a given treatment, machine learning can help advance the development of personalized medicine [30]. By avoiding pointless therapies and lowering the possibility of unfavorable outcomes, this strategy known as precision medicine, and it has the potential to improve patient outcomes and lower healthcare expenditures [31].

4. Discussion

The study's findings demonstrate that artificial intelligence and machine learning are crucial to many facets of pharmaco-epidemiology clinical research and medication development. By identifying patient subpopulations that are more likely to respond to particular medications, these technologies have the potential to enhance patient outcomes and provide more tailored treatment plans [29]. The use of Artificial Intelligence and machine learning has significantly improved the safety of conducting clinical research by enabling the detection of safety hazards and adverse medication reactions that were previously unknown or overlooked [29].

Drug development is time-consuming, expensive, and has a low success rate during the pre-clinical trials stage. However, by using automating procedures, raising productivity, and increasing predictability artificial intelligence and machine learning can aid in enhancing the effectiveness of drug development [32]. Researchers can more effectively and successfully conduct clinical trials by identifying patient subpopulations that are more likely to respond to a particular treatment and any potential safety concerns using artificial intelligence and machine learning algorithms to analyze large and complicated data [27]. Additionally, artificial intelligence and machine learning may accelerate the development of new drugs by extracting information from the vast amounts of data generated by various sources, including unstructured data that can be analyzed using natural language processing [33]. Modern machine learning algorithms have been created to handle massive data from genomics, imaging, and wearable technology, and they can be utilized to find drug candidates that have a higher likelihood of being effective [34]. Through the use of these techniques, it might be possible to pinpoint patient subgroups that would benefit more from specific treatments than others, enabling more individualized and precise medicine [28].

From the preliminary screening of pharmacological compounds to the prediction of success rates based on biological parameters, machine learning is a useful tool in R&D at various stages of early drug discovery [35]. Pharmaceutical companies can reduce the time and expense involved in generating medications by using machine learning to analyze data from experimental and manufacturing operations

[36]. Machine learning can also be useful in identifying novel chemicals or repurposing existing drugs to treat rare diseases or epidemics in cases where time is of the essence.

Machine Learning is revolutionizing the medical industry, from fundamental research to clinical applications, bringing about a paradigm shift [12]. However, it is crucial to exercise caution when implementing machine learning in practice. The technology may be vulnerable in areas like protecting against hostile assaults and assuring the security of data [37]. Adversarial assaults are especially worrisome since they could cause a total misdiagnosis that could be used for fraudulent activities by manipulating input data with malice [38]. These vulnerabilities present a real threat but can be mitigated with sufficient effort and attention.

The incorporation of machine learning into medical applications has the potential to transform the profession by analyzing massive volumes of data and producing effective solutions that can help both physicians and patients. Increased integration presents several opportunities to improve treatment effectiveness while lowering costs [36]. However, the biggest obstacle is combining enormous volumes of big data from genomes, transcriptomics, proteomics, and metabolomics with complex systems science, systems biology, and systems medicine to get the best outcomes [7]. For system-level interventions, such as bettering patient selection and recruiting for clinical trials, lowering readmission rates, and automating patient follow-up to track complications, machine learning, and artificial learning are critical for pharmaco-epidemiology and in turn, play a significant role in public health. However, more research is required to fully utilize the benefits of machine learning and artificial learning in pharmaco-epidemiology.

5. Conclusion

The role of Artificial Intelligence (AI) and Machine Learning (ML) in pharmaco-epidemiology holds potential and promises significant advancements in understanding medication safety and effectiveness. The application of AI and ML techniques can facilitate the discovery of adverse drug events, aid in the identification of high-risk patient populations, and streamline post-marketing surveillance. Furthermore, the utilization of these technologies in dealing with large data sets can enhance the efficiency and accuracy of clinical and pre-clinical trials thereby, ensuring the timely detection of medication-related risks. As AI and ML continue to evolve, it is crucial for researchers and healthcare professionals to make use of them to embrace their plans achieving full potential for improving public health and patient outcomes. While challenges lie ahead, the rapid development in Artificial Intelligence and Machine Learning, the pharmaceutical-epidemiological field is set for a new era of transformation that will benefit not only healthcare providers but also patients.

6. Declarations

6.1 Conflict of Interest Statement

The authors have no conflict of interests to declare.

6.2 Funding Disclosure

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7. References

1. Bohr, H. (2020). Drug discovery and molecular modeling using Artificial Intelligence. *Artificial Intelligence in Healthcare*, 61–83. <https://doi.org/10.1016/b978-0-12-818438-7.00003-4>
2. Harrer, S., Shah, P., Antony, B., & Hu, J. (2019). Artificial Intelligence for Clinical Trial Design. *Trends in Pharmacological Sciences*, 40(8), 577–591. <https://doi.org/10.1016/j.tips.2019.05.005>.
3. Bali, J., Garg, R., & Bali, R. T. (2019). Artificial Intelligence (AI) in Healthcare and biomedical research: Why a strong computational/ai bioethics framework is required? *Indian Journal of Ophthalmology*, 67(1), 3. https://doi.org/10.4103/ijo.ijo_1292_18
4. Radivojević, T., Costello, Z., Workman, K., & Garcia Martin, H. (2020). A machine learning automated recommendation tool for Synthetic Biology. *Nature Communications*, 11(1). <https://doi.org/10.1038/s41467-020-18008-4>
5. Ahmed, Z., Mohamed, K., Zeeshan, S., & Dong, X. Q. (2020). Artificial Intelligence with multi-functional machine learning platform development for better healthcare and Precision Medicine. *Database*, 2020. <https://doi.org/10.1093/database/baaa010>
6. Tang, T. T., Zawaski, J. A., Francis, K. N., Qutub, A. A., & Gaber, M. W. (2019). Image-based classification of tumor type and growth rate using Machine Learning: A Preclinical Study. *Scientific Reports*, 9(1). <https://doi.org/10.1038/s41598-019-48738-5>
7. West, C. M. L., Dunning, A. M., & Rosenstein, B. S. (2012). Genome-wide association studies and prediction of normal tissue toxicity. *Seminars in Radiation Oncology*, 22(2), 91–99. <https://doi.org/10.1016/j.semradonc.2011.12.007>
8. Kang, L., Duan, Y., Chen, C., Li, S., Li, M., Chen, L., & Wen, Z. (2022). Structure-activity relationship (SAR) model for predicting teratogenic risk of antiseizure medications in pregnancy by using support vector machine. *Frontiers in Pharmacology*, 13. <https://doi.org/10.3389/fphar.2022.747935>.
9. Bouhedjar, K., Boukelia, A., Khorief Nacereddine, A., Boucheham, A., Belaidi, A., & Djerourou, A. (2020). A natural language processing approach based on embedding deep learning from heterogeneous compounds for quantitative structure–activity relationship modeling. *Chemical Biology & Drug Design*, 96(3), 961–972. <https://doi.org/10.1111/cbdd.13742>.
10. Ghosh, B., & Choudhuri, S. (2021). Drug design for malaria with Artificial Intelligence (AI). *Plasmodium Species and Drug Resistance*. <https://doi.org/10.5772/intechopen.98695> .
11. Sessa, M., Khan, A. R., Liang, D., Andersen, M., & Kulahci, M. (2020). Artificial Intelligence in Pharmacoepidemiology: A systematic review. part 1—overview of Knowledge Discovery Techniques in artificial intelligence. *Frontiers in Pharmacology*, 11. <https://doi.org/10.3389/fphar.2020.01028>

12. Schwartz, R. P., Kelly, S. M., Mitchell, S. G., O'Grady, K. E., Sharma, A., & Jaffe, J. H. (2020). Methadone treatment of arrestees: A randomized clinical trial. *Drug and Alcohol Dependence*, 206, 107680. <https://doi.org/10.1016/j.drugalcdep.2019.107680>
13. Stanfill, M. H., & Marc, D. T. (2019). Health Information Management: Implications of artificial intelligence on healthcare data and Information Management. *Yearbook of Medical Informatics*, 28(01), 056–064. <https://doi.org/10.1055/s-0039-1677913>
14. Zhang, W.-W., Li, L., Li, D., Liu, J., Li, X., Li, W., Xu, X., Zhang, M. J., Chandler, L. A., Lin, H., Hu, A., Xu, W., & Lam, D. M.-K. (2018). The first approved gene therapy product for cancer ad-p53(gendicine): 12 years in the clinic. *Human Gene Therapy*, 29(2), 160–179. <https://doi.org/10.1089/hum.2017.218>
15. Krakow, E. F., Hemmer, M., Wang, T., Logan, B., Arora, M., Spellman, S., Couriel, D., Alousi, A., Pidala, J., Last, M., Lachance, S., & Moodie, E. E. (2017). Tools for the Precision Medicine Era: How to develop highly personalized treatment recommendations from cohort and registry data using Q-Learning. *American Journal of Epidemiology*, 186(2), 160–172. <https://doi.org/10.1093/aje/kwx027>.
16. Obermeyer, Z., & Emanuel, E. J. (2016). Predicting the future — Big Data, machine learning, and clinical medicine. *New England Journal of Medicine*, 375(13), 1216–1219. <https://doi.org/10.1056/nejmp1606181>
17. Lebedev, G., Fartushnyi, E., Fartushnyi, I., Shaderkin, I., Klimenko, H., Kozhin, P., Koshechkin, K., Ryabkov, I., Tarasov, V., Morozov, E., & Fomina, I. (2020). Technology of supporting medical decision-making using evidence-based medicine and Artificial Intelligence. *Procedia Computer Science*, 176, 1703–1712. <https://doi.org/10.1016/j.procs.2020.09.195>
18. DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. *Journal of Health Economics*, 47, 20–33. <https://doi.org/10.1016/j.jhealeco.2016.01.012>
19. Wong, C. H., Siah, K. W., & Lo, A. W. (2019). Estimation of clinical trial success rates and related parameters. *Biostatistics*, 20(2), 273–286. <https://doi.org/10.1093/biostatistics/kxx069>
20. Azzolina, D., Baldi (University of Padova), I., Barbati, G., Berchiolla, P., Bottigliengo, D., Bucci, A., Calza, S., Dolce, P., Edefonti, V., Faragalli, A., Fiorito, G., Gandin, I., Giudici, F., Gregori, D., Gregorio, C., Ieva, F., Lanera, C., Lorenzoni, G., Marchioni, M., ... Vezzoli, M. (2022). Machine learning in clinical and epidemiological research: Isn't it time for Biostatisticians to work on it? *Epidemiology, Biostatistics, and Public Health*, 16(4). <https://doi.org/10.2427/13245>
21. Kolluri, S., Lin, J., Liu, R., Zhang, Y., & Zhang, W. (2022). Machine Learning and Artificial Intelligence in Pharmaceutical Research and Development: A Review. *The AAPS Journal*, 24(1). <https://doi.org/10.1208/s12248-021-00644-3>.
22. Esteva, A., Kuprel, B., Novoa, R. A., Ko, J., Swetter, S. M., Blau, H. M., & Thrun, S. (2017). Dermatologist-level classification of skin cancer with Deep Neural Networks. *Nature*, 542(7639), 115–118. <https://doi.org/10.1038/nature21056>.

23. Fabris, A., Bruschi, M., Santucci, L., Candiano, G., Granata, S., Dalla Gassa, A., Antonucci, N., Petretto, A., Ghiggeri, G. M., Gambaro, G., Lupo, A., & Zaza, G. (2017). Proteomic-based research strategy identified laminin subunit alpha 2 as a potential urinary-specific biomarker for the medullary sponge kidney disease. *Kidney International*, 91(2), 459–468. <https://doi.org/10.1016/j.kint.2016.09.035>.
24. Réda, C., Kaufmann, E., & Delahaye-Duriez, A. (2020). Machine learning applications in drug development. *Computational and Structural Biotechnology Journal*, 18, 241–252. <https://doi.org/10.1016/j.csbj.2019.12.006>.
25. Schork, N. J. (2019). Artificial Intelligence and personalized medicine. *Precision Medicine in Cancer Therapy*, 265–283. https://doi.org/10.1007/978-3-030-16391-4_11
26. de Manzoni, G., Marrelli, D., Verlato, G., Morgagni, P., & Roviello, F. (2015). Western perspective and epidemiology of Gastric Cancer. *Gastric Cancer*, 111–123. https://doi.org/10.1007/978-3-319-15826-6_7.
27. Stokes, J. M., Yang, K., Swanson, K., Jin, W., Cubillos-Ruiz, A., Donghia, N. M., MacNair, C. R., French, S., Carfrae, L. A., Bloom-Ackermann, Z., Tran, V. M., Chiappino-Pepe, A., Badran, A. H., Andrews, I. W., Chory, E. J., Church, G. M., Brown, E. D., Jaakkola, T. S., Barzilay, R., & Collins, J. J. (2020). A deep learning approach to antibiotic discovery. *Cell*, 180(4). <https://doi.org/10.1016/j.cell.2020.01.021>
28. Chen, P.-H. C., Liu, Y., & Peng, L. (2019). How to develop machine learning models for Healthcare. *Nature Materials*, 18(5), 410–414. <https://doi.org/10.1038/s41563-019-0345-0>.
29. Shimoda, A., Ichikawa, D., & Oyama, H. (2018). Prediction models to identify individuals at risk of metabolic syndrome who are unlikely to participate in a Health Intervention Program. *International Journal of Medical Informatics*, 111, 90–99. <https://doi.org/10.1016/j.ijmedinf.2017.12.009>
30. Gams, M., Horvat, M., Ožek, M., Luštrek, M., & Gradišek, A. (2014). Integrating artificial and human intelligence into tablet production process. *AAPS PharmSciTech*, 15(6), 1447–1453. <https://doi.org/10.1208/s12249-014-0174-z>.
31. Saria, S., Butte, A., & Sheikh, A. (2018). Better Medicine Through Machine Learning: What’s real, and what’s artificial? *PLOS Medicine*, 15(12). <https://doi.org/10.1371/journal.pmed.1002721>
32. Chan, H. C. S., Shan, H., Dahoun, T., Vogel, H., & Yuan, S. (2019). Advancing Drug Discovery via Artificial Intelligence. *Trends in Pharmacological Sciences*, 40(8), 592–604. <https://doi.org/10.1016/j.tips.2019.06.004>
33. Liu, B., He, H., Luo, H., Zhang, T., & Jiang, J. (2019). Artificial Intelligence and big data facilitated targeted drug discovery. *Stroke and Vascular Neurology*, 4(4), 206–213. <https://doi.org/10.1136/svn-2019-000290>

34. Arsalan, T., Koshechkin, K., & Lebedev, G. (2020). Scientific approaches to the digitalization of drugs assortment monitoring using artificial neural networks. *Intelligent Decision Technologies*, 391–401. https://doi.org/10.1007/978-981-15-5925-9_33
35. Denecke, K., Gabarron, E., Grainger, R., Konstantinidis, S. T., Lau, A., Rivera-Romero, O., Miron-Shatz, T., & Merolli, M. (2019). Artificial Intelligence for Participatory Health: Applications, impact, and future implications. *Yearbook of Medical Informatics*, 28(01), 165–173. <https://doi.org/10.1055/s-0039-1677902>
36. Churpek, M. M., Yuen, T. C., Winslow, C., Meltzer, D. O., Kattan, M. W., & Edelson, D. P. (2016). Multicenter comparison of machine learning methods and conventional regression for predicting clinical deterioration on the wards. *Critical Care Medicine*, 44(2), 368–374. <https://doi.org/10.1097/ccm.0000000000001571>.
37. Abdellaoui, R., Foulquié, P., Texier, N., Faviez, C., Burgun, A., & Schück, S. (2018). Detection of cases of noncompliance to drug treatment in patient forum posts: Topic model approach. *Journal of Medical Internet Research*, 20(3). <https://doi.org/10.2196/jmir.9222>
38. Kim, H.-J., Han, D., Kim, J.-H., Kim, D., Ha, B., Seog, W., Lee, Y.-K., Lim, D., Hong, S. O., Park, M.-J., & Heo, J. N. (2020). An easy-to-use machine learning model to predict the prognosis of patients with COVID-19: Retrospective cohort study. *Journal of Medical Internet Research*, 22(11). <https://doi.org/10.2196/24225>