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How AI and Machine Learning Stand for Used in Keeping an Eye on Drug Safety a Review Article

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Abstract: Pharmacovigilance, as explained by the World Health Organization (WHO), involves various activities aimed at spotting and preventing any drug-related issues. Because there are many drug safety incidents, pharmaceutical companies and government health agencies believe that these activities are crucial for keeping patients safe. One major goal is to quickly find adverse drug events (ADEs), which are harmful effects that happen when a patient takes a medicine and might be caused by the drug. Artificial intelligence, using machine learning, employs algorithms and past knowledge to make predictions. Lately, there has been a growing interest in using more artificial intelligence in monitoring the safety of medicines already on the market and those in development. This study aimed to uncover and explain how artificial intelligence is used in pharmacovigilance by reviewing existing literature. We conducted a detailed analysis to compare the pros and cons of machine learning and deep learning, especially in tasks like identifying entities and classifying relationships related to ADE extraction. Furthermore, we looked at specific features and how they affect the performance of these methods. Broadly, our research also explored extracting ADEs from different sources like scientific papers, social media, and drug labels, not just relying on machine learning or deep learning alone.

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I. INTRODUCTION

The origins of pharmacovigilance date back to the mid-19th century, specifically in 1848, when the first recorded fatal reaction was observed after a young patient underwent chloroform anaesthesia.(1)A major turning point occurred in 1937 with the sulfanilamide elixir tragedy in the United States. The use of diethylene glycol as a solvent resulted in over 100 fatalities, which led to the enactment of the Food, Drug, and Cosmetic Act of 1938 and the implementation of more stringent drug safety regulations.(2)The most significant turning point in the history of drug safety was the thalidomide tragedy of 1961. This incident resulted in thousands of severe birth defects globally and highlighted the critical necessity for systematic post-marketing surveillance.(1)In response, the United States enacted the Kefauver-Harris Amendments in 1962, which required evidence of both safety and efficacy before any drug could gain approval. Similarly, the United Kingdom launched the Yellow Card Scheme in 1964, becoming one of the first formal systems for reporting spontaneous adverse drug reactions.(2)At the global level, the World Health Organization (WHO) initiated the Program for International Drug Monitoring in 1968. This initiative received further support from the Uppsala Monitoring Centre in 1978, which continues to manage the international adverse drug reaction database known as VigiBase. (3)These initiatives established the groundwork for contemporary pharmacovigilance, which has evolved into organized national programs in numerous countries, as well as regional platforms like EudraVigilance within the European Union. This evolution has turned drug safety into a collaborative global endeavour.(1)

Pharmacovigilance employs a variety of complementary strategies aimed at detecting, assessing, and preventing adverse drug reactions (ADRs). The most conventional approach is passive pharmacovigilance, which depends on *spontaneous reporting systems (SRS)*. In this system, healthcare professionals, patients, or manufacturers voluntarily submit reports of ADRs. While this method is cost-effective and crucial for signal detection, it does have significant drawbacks, including under-reporting and reporting bias.(4)

To address these weaknesses, methods such as targeted spontaneous reporting and stimulated reporting have been implemented. These approaches concentrate on specific populations, high-risk medications, or promote reporting following safety alerts.(5)In contrast, active pharmacovigilance utilizes systematic and proactive approaches, including cohort event monitoring, sentinel surveillance, and patient registries. These methods actively gather data from predetermined patient groups, offering more reliable and comprehensive safety information.(6)These approaches require significant resources, yet they are essential for detecting rare and delayed adverse drug

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reactions (ADRs) that passive systems frequently overlook. In addition to surveillance, observational epidemiological studies—including cohort, case-control, and cross-sectional designs—aid in both generating and testing hypotheses. This enables a thorough evaluation of causal relationships between drug exposure and adverse outcomes.(7)Furthermore, post-marketing surveillance programs, required by regulatory agencies, incorporate both passive and active techniques. They increasingly utilize electronic health records, real-world data, and automated data mining tools for effective signal detection.(8)Together, these strategies create a thorough framework in pharmacovigilance. This ensures the ongoing assessment of the benefit–risk balance throughout a drug's lifecycle, ultimately protecting patient safety world wide. An efficient pharmacovigilance (PV) system is defined by several essential characteristics that prioritize patient safety and drug effectiveness. Firstly, it must facilitate thorough data collection from a variety of sources, including spontaneous reports, electronic health records, and social media, in order to capture a broad spectrum of adverse drug reactions (ADRs).(9) Secondly, the timely detection of signals is essential. It enables the quick identification of potential safety issues through advanced analytical techniques, which in turn supports prompt risk assessment and regulatory intervention.(10)Thirdly, transparent reporting mechanisms must be in place, providing clear and accessible channels for healthcare professionals and patients to report ADRs, fostering trust and engagement in the PV process.(11)

Moreover, complying with regulatory standards and international guidelines, such as those set forth by the World Health Organization (WHO), enhances the credibility and effectiveness of pharmacovigilance (PV) activities.(12) Continuous education and training for both healthcare providers and patients boosts awareness of adverse drug reaction (ADR) reporting procedures, thereby reinforcing the overall system.(13) Integrating with healthcare infrastructure, such as electronic health records and clinical decision support systems, enhances data accuracy and accessibility.(14) A robust PV system ultimately embraces an ethical and patient-centric approach, placing patient welfare at the forefront of all safety monitoring and decision-making processes.(15) The characteristics of pharmacovigilance systems empower them to efficiently monitor, identify, and prevent adverse drug events, thereby ensuring the highest level of patient safety and positive public health outcomes. The emergence of artificial intelligence (AI) and machine learning (ML) has revolutionized pharmacovigilance. These technologies facilitate the analysis of extensive healthcare data, such as electronic health records, social media reports, and real-world evidence, allowing for the more efficient and accurate detection of safety signals.(9)

AI-driven algorithms are capable of recognizing patterns, forecasting potential Adverse Drug Reactions (ADRs), and enhancing regulatory decision-making, thereby complementing traditional Pharmacovigilance (PV) methods. International partnerships, including the WHO Program for International Drug Monitoring and the Uppsala Monitoring Centre, have established standardized methodologies, encouraged global ADR reporting, and contributed to improving patient safety on a global scale. (3) Overall, pharmacovigilance combines clinical, regulatory, and technological strategies to ensure the safe and rational use of medications. It serves as a crucial foundation of contemporary healthcare systems, playing a vital role in protecting public health.

The growing complexity and vastness of healthcare data have posed significant challenges for traditional pharmacovigilance systems, making it increasingly difficult to identify rare, delayed, or intricate adverse drug reactions promptly. To overcome these hurdles, artificial intelligence (AI) and machine learning (ML) techniques have been incorporated into pharmacovigilance processes, allowing for more efficient and precise analysis of extensive datasets. AI algorithms can autonomously scan various sources, including electronic health records, social media posts, spontaneous reporting databases, and other real-world data, to uncover potential safety signals that conventional methods may overlook.(9) Machine learning models, such as natural language processing and predictive analytics, are especially valuable for identifying patterns, forecasting adverse events, and evaluating the severity and causation of drug reactions.(10) Pharmacovigilance integrates clinical, regulatory, and technological strategies to ensure the safe and rational use of medications, forming a crucial pillar of modern healthcare systems. The incorporation of AI and ML in pharmacovigilance marks a significant transformation, allowing for more proactive, predictive, and comprehensive monitoring of drug safety. This progress ultimately improves patient outcomes and supports public health.

Signal detection serves as a fundamental aspect of pharmacovigilance, focusing on the discovery of new or previously unrecognized adverse drug reactions (ADRs). Recent advancements in statistical methods and data mining techniques have greatly improved the capacity to identify safety signals. Tools like disproportionality analysis and Bayesian data mining techniques are frequently employed to examine extensive pharmacovigilance databases. These approaches have enhanced both the sensitivity and specificity of signal detection, facilitating quicker identification of potential safety issues.

II. IMPORTANCE OF PHARMACOVIGILANCE IN HEALTHCARE

Pharmacovigilance (PV) has emerged as a fundamental aspect of contemporary healthcare, serving a crucial function in safeguarding drug safety, protecting patients, and fostering public trust in therapeutic treatments. Essentially, pharmacovigilance focuses on the detection, assessment, understanding, and prevention of adverse drug reactions (ADRs) along with other issues related to medications. Clinical trials play a crucial role in determining a treatment's efficacy and initial safety; however, they frequently face limitations such as small sample sizes, brief durations, and stringent inclusion criteria. Consequently, rare, long-term, or population-specific adverse effects often go unnoticed until the medications are used broadly in real-world settings.(16)In this context, pharmacovigilance plays a vital role by offering

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ongoing, post-marketing surveillance. This ensures the timely detection of safety signals and the effective management of potential risks.

One of the key contributions of Pharmacovigilance (PV) to healthcare is its role in decreasing drug-related morbidity and mortality. Adverse Drug Reactions (ADRs) are a major factor in hospital admissions and healthcare expenses worldwide, yet under-reporting continues to be a significant hurdle. Hazell and Shakir (2006) highlighted in their systematic review that the widespread under-reporting of ADRs hampers the timely identification of safety issues. By promoting spontaneous reporting, active monitoring, and the involvement of healthcare professionals, PV systems gather valuable real-world data that not only improve patient safety but also guide clinical decision-making.(4)

Pharmacovigilance also serves a crucial role in regulation and policy development. Global health organizations, including the European Medicines Agency (EMA) and the World Health Organization (WHO), depend on pharmacovigilance data to inform decisions regarding labelling modifications, risk management strategies, and, when required, product withdrawals.(17) These activities are essential for upholding public trust in medications and vaccination initiatives, particularly following health crises like the COVID-19 pandemic. The swift development and distribution of vaccines necessitated improved safety monitoring.(1) Pharmacovigilance has transformed from a reactive system into a proactive instrument for protecting public health. This evolution involves the systematic collection, analysis, and dissemination of safety information.

The future of pharmacovigilance in healthcare is poised to flourish through the integration of advanced technologies and real-world data. As polypharmacy and intricate therapies like biologics and gene-based medicines become more prevalent, traditional methods of detecting adverse drug reactions (ADRs) may fall short. Recent developments in big data analytics, artificial intelligence (AI), and natural language processing have demonstrated potential in enhancing both the timeliness and accuracy of signal detection.(18) These data-driven methods facilitate the examination of extensive and varied datasets—spanning spontaneous reporting systems, electronic health records, and even social media. This provides fresh opportunities to identify rare, intricate, or population-specific safety concerns.

Pharmacovigilance is vital to the healthcare sector as it protects patients, bolsters regulatory decision-making, improves clinical practices, and responds to new challenges through innovation. Its significance goes beyond mere regulatory compliance; it embodies an ethical duty for healthcare providers and serves as a cornerstone for sustainable, patient-cantered healthcare systems.

III. IMPORTANCE OF PHARMACOVIGILANCE IN THE PHARMACY FIELD

Pharmacovigilance is crucial in the pharmacy sector, ensuring the safety, effectiveness, and appropriate use of medications throughout their entire lifecycle. This practice facilitates the systematic detection, evaluation, and prevention of adverse drug reactions (ADRs), which rank among the primary causes of morbidity and mortality globally.(19) In the field of pharmacy, pharmacovigilance enhances clinical decision-making by offering real-world evidence regarding drug safety. This crucial information complements pre-marketing clinical trial data, which frequently has limitations in identifying rare or long-term adverse effects.(20)

Pharmacists, as the most accessible healthcare professionals, play a vital role in pharmacovigilance activities. Their responsibilities include spontaneous reporting, patient counselling, medication error prevention, and participation in active surveillance programs.(21) Moreover, in the age of personalized medicine and polypharmacy—particularly among the elderly and those with chronic diseases—pharmacovigilance plays a crucial role in identifying drug–drug interactions and optimizing therapeutic regimens.(22) The incorporation of pharmacovigilance into pharmacy education and practice fosters patient trust and bolsters public health systems by minimizing drug-related hospitalizations and lowering healthcare expenses. Ultimately, pharmacovigilance transcends being merely a regulatory obligation; it embodies a professional and ethical duty within pharmacy practice, guaranteeing ongoing monitoring and the safe utilization of medicines across various populations.

Table 1 : This Table Highlights the Crucial Role of Pharmacovigilance Across Different Areas of Pharmacy Practice, Ensuring Patient Safety, Effective Drug Use, and Regulatory Compliance.(5,23)

Area in Pharmacy	Importance of Pharmacovigilance
Community Pharmacy	Detects and reports adverse drug reactions (ADRs) from patients using over-the-counter (OTC) and prescription drugs.
Hospital Pharmacy	Monitors and manages drug safety in inpatients, prevents medication errors, and supports safe therapeutic use.
Clinical Pharmacy	Provides evidence for optimizing drug therapy, minimizing drug interactions, and ensuring patient safety.
Industrial Pharmacy	Ensures continuous post-marketing surveillance of new drugs, biosimilars, and generics.

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Regulatory Pharmacy	Supplies safety data to regulatory authorities for drug approvals, labeling changes, or withdrawal decisions.
Academic & Research Pharmacy	Encourages studies on ADRs, risk management, and contributes to safer drug development.
Pharmacoeconomics	Reduces costs associated with ADRs, hospitalizations, and treatment failures.
Professional Responsibility	Builds trust between pharmacists, patients, and healthcare systems by ensuring drug safety.

Pharmacovigilance plays a vital role in healthcare, primarily focusing on patient safety and the identification of adverse drug reactions. It is essential in ensuring patient compliance and is also beneficial in pharmacogenomics for tailored medication.

- *Methods of Pharmacovigilance*

The activities associated with pharmacovigilance can generally be categorized into three main groups: regulatory, industry, and academia. Regulatory pharmacovigilance focuses on ensuring that medications are offered to the public with a favourable benefit-risk profile. In this context, we will explore several issues associated with regulatory post-marketing surveillance. This will be followed by an overview of the methods utilized to identify new Adverse Drug Reactions (ADRs) and a discussion of the advantages and disadvantages of each approach.(24)

- *Spontaneous Reporting*

As outlined earlier, spontaneous reporting serves as the primary method for detecting ADRs. Over the past few decades, this passive and cost-effective approach, used globally, has helped define the ADR profiles of numerous medications in everyday settings. However, a significant drawback of spontaneous reporting is the tendency for healthcare professionals to underreport cases. Recent studies indicate that underreporting can vary from 90% to 95%, depending on the drug, disease, and severity of the ADR.(25)

In 1961, a letter authored by Australian physician W.G. McBride was published in *The Lancet*. In this correspondence, he expressed his observation that infants born to mothers who had taken thalidomide during pregnancy were more frequently affected by congenital abnormalities compared to those who were not exposed to the drug in utero.(24) The primary responsibility of pharmacovigilance Centre is to gather and analyse reports, as well as to communicate potential risks to stakeholders when new signals of adverse drug reactions (ADRs) emerge. The pharmaceutical industry also employs spontaneous reporting to obtain information regarding their medications. Through a Spontaneous Reporting System (SRS), it becomes feasible to monitor all drugs on the market throughout their entire life cycle at a relatively low cost. However, a significant criticism of this method is the risk of selective reporting and underreporting.(25) Spontaneous reporting systems (SRS) are fundamental to pharmacovigilance globally, acting as the main tool for identifying new and rare adverse drug reactions (ADRs) post-marketing authorization. These systems depend on voluntary submissions from healthcare professionals, patients, and pharmaceutical companies. Historically, they have played a crucial role in uncovering significant safety signals, including those linked to thalidomide, rofecoxib, and cisapride. (26)

According to Härmark and van Grootheest (2008), Spontaneous Reporting Systems (SRS) hold significant value due to their coverage of large and diverse patient populations, their cost-effectiveness, and their capacity for ongoing monitoring during a drug's life cycle. Nevertheless, there are limitations such as considerable underreporting, reporting bias, and inconsistent data quality, which can undermine the strength of causal inference. Recent advancements are focused on enhancing spontaneous reporting by incorporating patient reports, electronic health records, and data-mining techniques to improve signal detection.(24,27)

Furthermore, regulatory bodies like the WHO's Uppsala Monitoring Centre and the European Medicines Agency have established global and regional databases. These initiatives facilitate harmonization and extensive analyses across various countries. Despite certain limitations, spontaneous reporting remains essential for the early identification of unexpected adverse drug reactions (ADRs) and serves as the foundation for complementary pharmacovigilance methods.

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Table 2. Overview of Major International Spontaneous Reporting Databases that can be Queried Through Publicly Available Online Tools

Database	Time window	Products covered	Catchment area	Search criteria (customization)
FDA Adverse Event Reporting System (FAERS)	1969 – present	Medicines *	Worldwide (20 million reports)	By medication (up to five)/reaction #. Raw data can also be downloaded $
WHO – VigiBase	1968 – present	Medicines and vaccines	Worldwide (over 110 countries)	By product
Eudravigilance	2001 – present	Medicines authorized in the European Union ±	Europe	By product/substance
Australian Database of Adverse Event Notifications (DAEN)	1971 – present	Medicines and vaccines licensed in Australia	Australia	By product, date range, organ/system/toxicity
Canada Vigilance Adverse Reaction Online Database	1965 – present	Medicines, vaccines, and health products licensed in Canada	Canada	By product, date, seriousness, demographic information, ADR term

Outlines major international spontaneous reporting databases used in pharmacovigilance, including FAERS, WHO-VigiBase, Eudravigilance, DAEN, and Canada Vigilance. It highlights their coverage, time span, geographic scope, and search customization. These databases provide accessible real-world safety data, supporting early detection of adverse drug reactions and proactive clinical monitoring worldwide. (33)

➢ *Intensive Monitoring Studies in Pharmacovigilance*

In the late 1970s and early 1980s, New Zealand and the UK introduced a novel form of active surveillance. This included the Intensive Medicines Monitoring Program in New Zealand and Prescription Event Monitoring in the UK. These comprehensive monitoring systems utilize prescription data to identify individuals using specific medications. The prescriber is then consulted regarding any adverse events that may arise during the medication's use. The collected data is analyzed to detect new signals. Detailed descriptions of the methodologies employed in these intensive monitoring systems can be found in other sources.(28,29) The primary responsibility of the pharmacovigilance center is to gather and analyze reports, while also informing stakeholders about potential risks associated with emerging signals of new adverse drug reactions (ADRs). The pharmaceutical industry utilizes spontaneous reporting to gather information regarding their medications. Through a Spontaneous Reporting System (SRS), it's feasible to monitor all drugs on the market throughout their entire life cycle at a relatively low cost. However, a significant criticism of this method is the risk of selective reporting and underreporting.(30)

Intensive Monitoring Studies (IMS) are essential for post-marketing pharmacovigilance, as they focus on the active collection of real-world data regarding adverse drug reactions (ADRs). These studies aim to identify rare or previously unrecognized ADRs that might not be detected during pre-marketing clinical trials. IMS generally consist of systematic, longitudinal data collection from healthcare environments, such as hospitals or general practices. They often employ methodologies like Prescription Event Monitoring (PEM) or Cohort Event Monitoring (CEM).(31)

A systematic review conducted by Torre et al. (2019) examined 69 Integrated Monitoring Studies (IMS) across 26 countries, emphasizing their effectiveness in detecting Adverse Drug Reactions (ADRs) and guiding regulatory decisions. The review highlighted that, while IMS offer valuable insights into drug safety, they can be resource-intensive and may face limitations such as underreporting and the absence of control groups.(32)

Despite these obstacles, IMS continue to be a fundamental element in producing real-world evidence on drug safety, serving as a complement to spontaneous reporting systems and enhancing the overall landscape of pharmacovigilance.(32) Furthermore, innovations in digital health technologies and data analytics are improving the efficiency and reach of Integrated Management Systems (IMS), allowing for more thorough monitoring of Adverse Drug Reactions (ADRs) across various populations.

➢ *Prescription Event Monitoring (PEM)*

Prescription Event Monitoring (PEM) is among the earliest and most commonly utilized traditional methods of pharmacovigilance. It is specifically designed to actively track the safety of newly launched medications within real-world clinical settings. Originating in the United Kingdom, the Prescription Event Monitoring (PEM) system utilizes prescription data to identify groups of patients who have been exposed to a specific drug. These patients are subsequently monitored prospectively for any adverse events th2tematic, population-based approach. This allows for the thorough collection of information regarding both serious and non-

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serious events. Review articles emphasize that Patient Experience Measures (PEM) have proven especially effective in identifying unexpected and delayed reactions, evaluating drug safety across various populations, and recognizing patterns of use beyond controlled trials.(19,34)

PEM employs a non-interventional observational cohort design to offer active surveillance of specific medications on a national level in England. Data collection starts right after marketing, providing valuable 'real-world' clinical information for the initial groups of patients who are prescribed the medication of interest within the community. The identification of these patients depends on data obtained from dispensed National Health Service (NHS) prescriptions. This information is securely provided to the DSRU under established agreements by a central NHS prescription processing center, referred to as the NHS Prescription Services.(35) Comparative studies reveal that only a small percentage of adverse events identified by Post-Exposure Monitoring (PEM) are also reported through spontaneous reporting systems. This highlights PEM's complementary role in enhancing pharmacovigilance capabilities.(36) Nevertheless, the literature highlights several limitations, including its resource-intensive nature, reliance on healthcare systems that maintain extensive prescribing databases, and diminished relevance in low- and middle-income countries.(37,38)

Table 3 : This Outline Presents a Step-by-Step framework for Patient Event Monitoring (PEM). It Covers the Entire Process, Starting from Drug Identification and Progressing Through Prescription Data, Patient Follow-up, Event Monitoring, Analysis, and Reporting for Pharmacovigilance.(39,40)

Stage	Activity	Details Collected
1. Identification	Select drug under surveillance	Name, formulation, date of market launch, indication
2. Prescription Data	Collect data from NHS prescriptions/other sources	GP details, date of first prescription, number of patients
3. Patient Enrollment	Patients automatically included after first prescription	Unique ID, age, sex, baseline demographics
4. Questionnaire Design	Prepare structured GP questionnaires	Time points: 3, 6, 12 months; baseline health, adverse events, comorbidities
5. Data Collection	Questionnaires sent to prescribing doctors	Clinical events, lab values, treatment outcomes, deaths (if any, with causes)
6. Event Monitoring	Adverse events tracked systematically	Serious adverse events (SAEs), non-serious adverse events, unexpected outcomes
7. Data Analysis	Statistical & epidemiological evaluation	Frequency, incidence, risk estimation, signal detection
8. Reporting	Generate pharmacovigilance & regulatory reports	Interim safety reports, regulatory submissions, publications
9. Feedback & Action	Communicate findings to stakeholders	Healthcare professionals, regulatory authorities, pharmaceutical companies

- *The Impact of Artificial Intelligence on Pharmacovigilance*

Artificial Intelligence (AI) is transforming pharmacovigilance by improving the detection, evaluation, and prevention of adverse drug reactions (ADRs). With the help of machine learning (ML) and natural language processing (NLP) algorithms, it is now possible to automate the analysis of extensive datasets, such as electronic health records, social media, and medical literature. This allows for the identification of potential safety signals far more efficiently than conventional approaches. AI enables real-time surveillance of drug safety, which allows for prompt interventions and informed regulatory decisions. Furthermore, AI-powered tools assist in automating case processing, thereby minimizing manual workload and lowering the chances of human error.(41,42)

- *Adverse Drug Detection & Monitoring*

Traditional methods for reporting and identifying adverse events play a crucial role in monitoring patient safety and pharmaceutical safety within healthcare settings. The initial approach, referred to as voluntary reporting, depends on healthcare providers, patients, and caregivers to inform regulatory agencies like the FDA or MHRA about any suspected adverse events associated with medications. This method provides valuable real-world data on adverse events

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that happen during regular clinical practice and is straightforward and easy to comprehend.(42,43) Artificial Intelligence (AI) is greatly advancing pharmacovigilance by enhancing the detection, assessment, and prevention of adverse drug reactions (ADRs).(41,44) Machine learning and natural language processing help computers automatically analyze large amounts of data, like electronic health records, social media posts, and medical articles. This makes it easier to spot safety issues compared to traditional ways.(45,42)

AI helps combine different types of data, making ADR detection systems more thorough. By examining big datasets, AI can find unknown ADRs and predict possible drug interactions, helping regulators make better decisions and keeping patients safer. Even with these improvements, using AI to spot adverse drug reactions (ADR) isn't without problems. Concerns about data privacy, the need for high-quality labeled datasets, and the difficulty in understanding how AI models work are big challenges. Tackling these issues is important for AI to be widely used in drug safety monitoring. To sum up, AI has a lot of potential to change how we detect and monitor adverse drug reactions, making it faster and more accurate. We need ongoing research to solve current problems and make the most of AI for better drug safety.

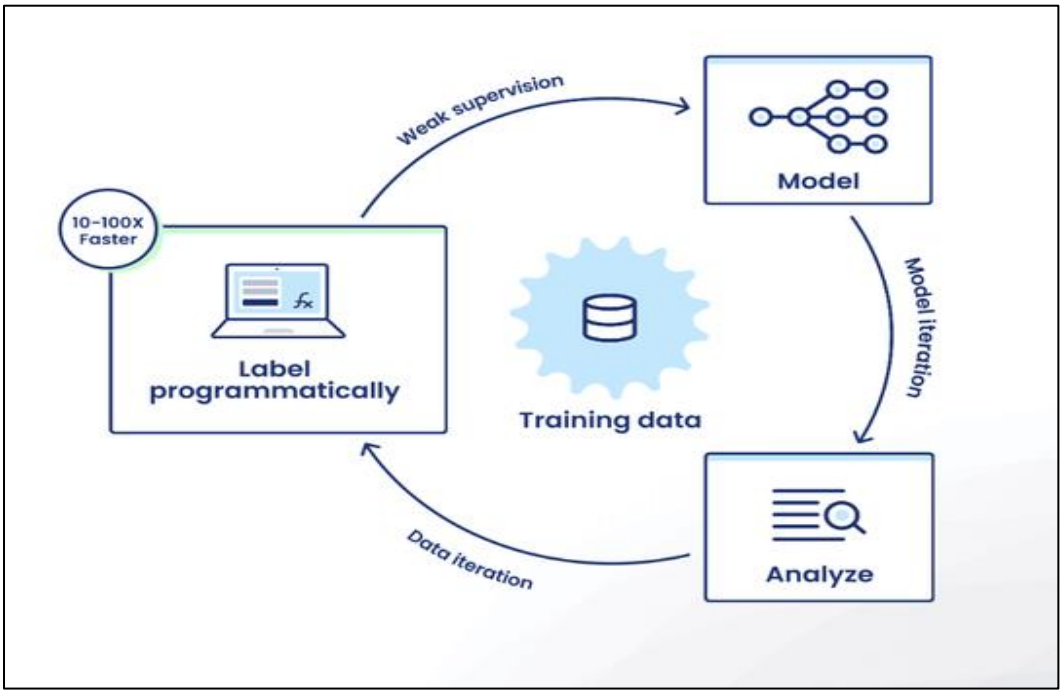

Fig 1 : This Image in Drug Safety Shows How AI and Machine Learning can Speed up the Process of Finding Bad Reactions to Medicines. By Quickly Adding Labels to Large Amounts of Data, Like Reports from Patients and Electronic Health Records, these Become Training Material for Computer Models. The Models then Study the Data to Spot Safety Issues, and the Findings Help Improve Both the Data and the Models. This Ongoing Process Makes Monitoring Medicine Reactions Quicker and more Precise.

- *Signal Detection and Risk Assessment*

Signal detection and risk assessment are crucial in monitoring drug safety because they help spot new or serious side effects that might not show up during clinical trials. Normally, we use specific statistical methods to analyze reports of these effects, but these methods can fall short due to issues like not all incidents being reported, delays in reporting, and challenges in handling large amounts of varied data.(46) Artificial Intelligence (AI), especially machine learning (ML) and natural language processing (NLP), has made it easier to automatically and quickly analyze large amounts of information from sources like health reports, social media, and medical articles. This helps in spotting unusual drug-related issues faster.(44,45)

AI models improve both sensitivity and specificity in detecting genuine safety signals while minimizing false positives. This enhancement significantly bolsters the reliability of risk assessment.(47) For instance, machine learning algorithms have the ability to learn continuously from a variety of datasets. They can predict the likelihood of adverse drug reactions (ADRs) in real-world scenarios, thereby facilitating early interventions and aiding in regulatory decision-making.(44) Despite these advancements, challenges such as model interpretability, variability in data quality, and regulatory acceptance remain significant, necessitating careful validation before integration into routine pharmacovigilance.(45,42)

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Table 3 : Summary of Articles Applying Supervised Machine Learning Methodologies to Signal Detection.(48)

Database(s) Used	ML Methods	Comparator(s)	Performance Metrics Reported	Key Findings
FDA Adverse Event Reporting System (FAERS)	Random Forest, Gradient Boosting, Neural Network, SVM	PRR, ROR, IC	AUROC, Precision, Recall	ML models outperformed traditional disproportionality methods.
Australia Pharmaceutical Benefit Scheme (Medication Dispensing Database)	Logistic Regression, Random Forest, Gradient Boosting	PRR, ROR	AUROC	Supervised ML detected ADRs more effectively than standard methods.
Korea Adverse Event Reporting System (KAERS)	Tree-based ML (Decision Trees, Random Forest, Gradient Boosting)	PRR, ROR	AUROC, Accuracy	Tree-based ML showed superior detection performance.
Ajou University Hospital EHR Database	Hybrid ML model combining algorithms	Standard disproportionality analysis	AUROC, Recall	Combining ML features improved ADR detection.
Netherlands Pharmacovigilance Centre Lareb	Multivariate Prediction Model	Clinical review	Sensitivity, Specificity	ML prioritized ICSRs requiring expert review.
FDA FAERS + Other Sources	Neural Networks, Gradient Boosting	PRR, IC	AUROC	Neural networks showed improved signal detection across datasets.
Korean EHR + Reporting Systems	Random Forest, SVM	PRR, ROR	AUROC, Precision	ML models achieved higher detection rates for lab-event-related ADRs.
US FDA FAERS	Gradient Boosting, Random Forest	PRR, ROR, IC	AUROC	ML outperformed disproportionality analysis in large-scale data.

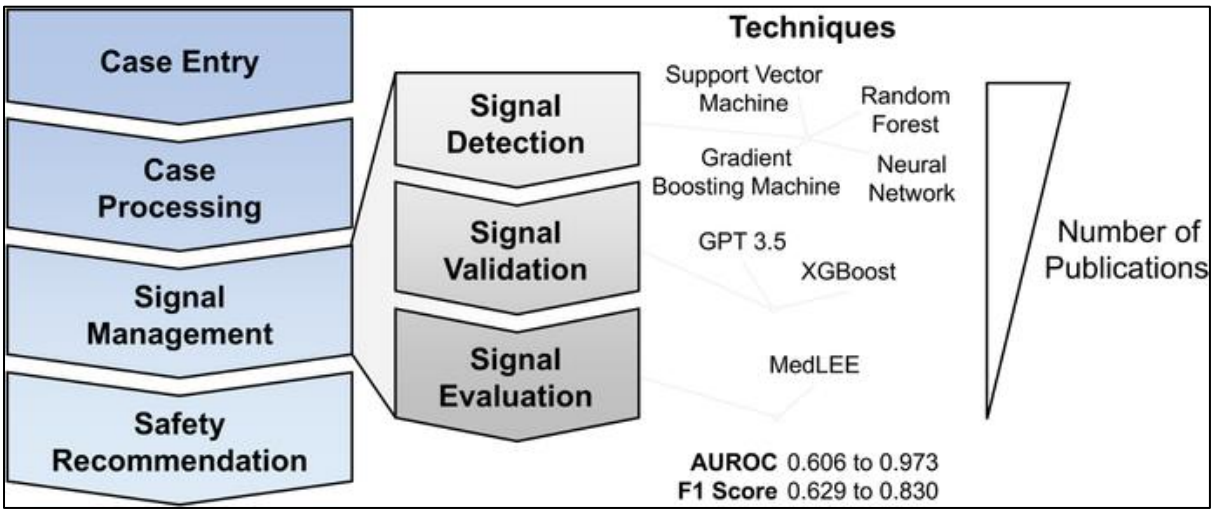

Fig 2 : The Figure Summarizes Studies on AI Applications in Pharmacovigilance Signal Management, Highlighting the Use of Supervised Machine Learning (e.g., Random Forest, Gradient Boosting) and NLP Tools

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➢ *Machine Learning in Pharmacovigilance: Enhancing Patient Safety Reports*

Machine learning has the potential to transform pharmacovigilance by efficiently analyzing unstructured text within patient safety reports. Evans and his team discovered that employing natural language processing (NLP) allows for the automatic classification of these texts, helping to assess the severity of harm. This method serves as a crucial safety measure to flag cases that could result in serious injury or death.

However, it's important to note that this approach is not flawless and cannot fully replace manual reviews at this stage. Additionally, the complex nature of medical language presents challenges that make this process difficult to execute effectively.(49)

Numerous studies have assessed the application of machine learning in the evaluation of patient safety reports, particularly within electronic health records. Marella et al. discovered that machine learning algorithms and text mining are effective techniques for screening and analyzing extensive semi-structured or unstructured data sets of adverse event and near-miss reports gathered via passive surveillance reporting systems. In a more targeted approach, Yang et al. developed a deep learning model that was tested on various data sets to detect allergic reactions within the free-text narratives of hospital safety reports, examining its generalizability.

The study showed that the model could help improve allergy care by allowing real-time monitoring for medical errors and system improvements. In the end, machine learning can be used in many ways to meet pharmacovigilance needs. This includes spotting important words in patient safety reports to prevent harm at clinical sites and tracking adverse drug reactions after drugs are marketed.(50)

➢ *Using Artificial Intelligence to Simulate Clinical Trials*

Chen and his team used machine learning with real-world data to mimic clinical trials for colorectal cancer and check for serious side effects. The risk ratios from these simulations were very similar to those from the actual trials. This shows that combining machine learning with real data could be very useful for simulating clinical trials.(50)

➢ *Opportunities for Future Research*

As artificial intelligence continues to be utilized across various sectors beyond healthcare, there are numerous avenues for future research into its application in pharmacovigilance. Upcoming studies could leverage databases that contain more complex input text or higher levels of 'noise' to assess whether AI technology can deliver accurate and efficient responses. When it comes to social media platforms, many articles have primarily focused on Twitter as their data source. However, other platforms, such as healthcare social networks, may provide valuable insights, especially given the growing interest in utilizing social media for pharmacovigilance in recent years.(51) Lastly, more studies on the potential cost savings in healthcare from automated machine learning methods could be useful.

IV. ADVANTAGES OF AI IN THE PHARMACOVIGILANCE

➢ *Early Signal Detection*

Artificial intelligence (AI) shows great promise in improving early signal detection in pharmacovigilance. Traditional statistical methods typically depend on disproportionality analysis, which can postpone the identification of safety issues. Conversely, AI and machine learning (ML) models combine data from spontaneous reporting systems, electronic health records (EHRs), and relevant literature to uncover hidden patterns and detect adverse drug reactions sooner. Deep learning techniques excel at recognizing subtle associations within extensive datasets that conventional tools might overlook.(52) Combining natural language processing (NLP) with data-mining techniques lets us automatically keep an eye on scientific articles and social media. This helps quickly spot new safety issues as they arise. These methods not only speed up the process of monitoring drug safety but also make it more accurate, helping to manage risks before they become bigger problems.(53)

➢ *Automation of Routine Tasks*

AI helps make routine drug safety tasks easier by automating them. This includes taking in cases, sorting them, and finding duplicates. Normally, these tasks need a lot of human effort, but AI can speed them up using natural language processing (NLP) and robotic process automation (RPA). For example, automated systems can pull important information from reports, cutting down on mistakes and saving time. Machine learning (ML).(54) AI models have improved the way we find duplicate reports in drug safety databases, doing a better job than older systems that follow set rules. Using automation helps reduce costs and lets drug safety experts spend more time on important tasks like assessing risks and making regulatory decisions.(4)

➢ *Predictive Analytics*

One of the most transformative advantages of AI in pharmacovigilance is its role in predictive analytics. By modeling complex interactions among drugs, diseases, and patient characteristics, AI can forecast potential adverse drug reactions (ADRs) before they manifest in large populations. Predictive algorithms based on EHR data and molecular structure similarity allow estimation of drug safety risks during early development phases.(55)Deep learning has significantly propelled this field forward by accurately predicting drug-drug interactions and off-target effects, which aids in both clinical decision-making and regulatory safety evaluations. Moreover, predictive models have been utilized to tailor drug safety monitoring, pinpointing patient subgroups that are at a greater risk for adverse drug reactions (ADRs).(56)

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➢ *Regulatory Compliance and Decision Support*

AI helps ensure that safety data reporting in drug monitoring is accurate, consistent, and prompt. Unlike manual processes, which can be slow and inconsistent, AI systems make it easier and faster to extract data, categorize it, and create reports.(60) Natural Language Processing (NLP) tools have the ability to convert unstructured reports into standardized vocabularies, such as MedDRA, which encourages uniform international reporting. Furthermore, machine learning (ML) powered platforms provide decision support by analyzing cumulative safety data and generating evidence for benefit-risk assessments. This functionality assists pharmaceutical companies in meeting their regulatory obligations.(58) Recent efforts have shown that AI can help make audits easier by improving how we track and document things, making sure we follow new safety rules like ICH E2B(R3) and FDA guidance. Using AI in these processes not only lowers the risk of not following the rules but also helps regulators and drug companies make better decisions based on solid evidence.(59)

➢ *Efficient Data Processing*

Artificial Intelligence (AI) has significantly enhanced the efficiency of data processing in pharmacovigilance systems. While the manual review of spontaneous reports and electronic health records (EHRs) can be tedious, Natural Language Processing (NLP) allows for the automated extraction of mentions of adverse events from unstructured clinical text, greatly alleviating the burden on human resources.(60) Large-scale clinical language models, like Gatortron, have significantly improved this process by efficiently accessing extensive amounts of EHR data with enhanced speed and accuracy. This advancement supports extensive pharmacovigilance efforts. Deep learning approaches have also been applied to real-time patient data streams, demonstrating the ability to continuously process information and predict safety events more rapidly than conventional methods(61). In addition, advanced machine learning techniques enable effective mining of diverse datasets, enhancing both the sensitivity and promptness of adverse drug reaction detection. Beyond structured clinical data, AI-powered text mining of social media allows for the efficient processing of vast patient-reported datasets, providing supplementary evidence for monitoring drug safety.(62) The combination of these advancements underscores the role of AI in facilitating scalable, swift, and accurate data processing, which in turn allows for earlier signal detection and more effective pharmacovigilance.

V. ETHICAL ISSUES OF ARTIFICIAL INTELLIGENCE IN PHARMACOVIGILANCE

Artificial intelligence (AI) is changing how we monitor drug safety. It helps automate tasks like data processing and risk prediction. While AI offers many benefits, it also brings challenges. These include worries about data privacy, fairness in algorithms, transparency, responsibility, and equal access. It's important to tackle these issues to make sure AI improves drug safety worldwide.

➢ *Data Privacy and Confidentiality*

One of the most urgent ethical challenges in AI-powered pharmacovigilance is the handling of sensitive patient information. Pharmacovigilance depends on a variety of data sources, such as electronic health records (EHRs), patient registries, genomic data, and, more recently, social media. Extracting information from these sources to identify adverse drug reactions (ADRs) poses considerable risks to confidentiality, especially if de-identification methods are not sufficiently robust.(63)

Even when datasets are anonymized, they can still be at risk of identifying individuals if they are compared with other data sources. This is particularly true in large networks that monitor drug safety. The risk increases with the growing use of cloud technology and sharing data across countries. Rules like the GDPR in the EU and HIPAA in the US provide important protections, but global drug safety efforts often involve sharing data between countries, which makes following these rules harder.(64) Using AI ethically in drug safety monitoring means we need clear ways to get permission, strong data protection, and strict rules in place. It's important for patients to trust that their personal information is used carefully and only for real health reasons.

➢ *Algorithmic Bias and Fairness*

Bias in AI models presents a significant ethical concern. The data utilized in these systems frequently emphasizes adults from affluent countries, leaving limited information regarding children, pregnant women, older individuals, and ethnic minorities. As a result, AI systems may struggle to accurately identify issues within these underrepresented groups.(65)

For instance, Gianfrancesco et al. illustrated how biases present in EHR-based machine learning models might result in unequal outcomes in healthcare predictions. In the context of pharmacovigilance, this could lead to the under-detection of adverse drug reactions (ADRs) among vulnerable populations, thereby worsening existing health disparities. Additionally, the dependence on spontaneously reported ADRs brings about further biases, as underreporting is prevalent and frequently affected by socioeconomic, cultural, and geographical factors.(4)To reduce bias, AI systems should utilize diverse datasets, undergo ongoing monitoring, and integrate fairness metrics in their evaluation processes. In the absence of these safeguards, there is a risk that AI could perpetuate systemic inequities instead of fostering inclusive drug safety.

➢ *Transparency and Clarity of Understanding*

AI models, especially those based on deep learning architectures, frequently face criticism as “black boxes” due to their opaque decision-making processes. In the field of pharmacovigilance, this absence of interpretability raises ethical concerns, as safety-related decisions—like identifying signals for regulatory review—need to be transparent and easily understandable.(66)Healthcare workers and regulators need clear reasons for labeling certain drugs as possible safety concerns. If AI insights aren't easy to understand, people may not trust them, making it harder to use them in official

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guidelines. Also, the EU's rules on AI and data protection emphasize the need for explanations about how decisions are made by algorithms.(67)

Creating explainable AI systems is crucial. Techniques like attention mechanisms, feature attribution, and rule-based hybrid models can enhance interpretability without compromising predictive accuracy. Moreover, ensuring transparency in AI poses not just a technical challenge but also an ethical obligation for fostering accountability and trust.

- *Accountability and Liability*

The integration of AI in pharmacovigilance brings forth complex legal and ethical dilemmas regarding accountability. In instances where an AI system fails to identify a significant adverse drug reaction (ADR) signal resulting in patient harm, questions arise about who should be held responsible—the pharmaceutical company, the software developer, or the regulatory authority. On the other hand, if AI produces false-positive signals, companies might endure unwarranted regulatory scrutiny, resulting in potential financial and reputational repercussions. (68) Currently, accountability frameworks are still in their early stages of development. Some advocate for shared responsibility models, where companies utilizing AI are required to validate and monitor their algorithms, while regulators offer oversight. However, as AI systems gain more autonomy, determining liability becomes increasingly complicated. It is essential to establish clear guidelines for accountability to prevent ethical ambiguity and safeguard patient protection.

- *Ethical Governance and Trust*

Finally, the responsible use of AI in pharmacovigilance necessitates strong governance frameworks. Trust is fundamental to pharmacovigilance, and any suspicion of AI misuse—such as unauthorized surveillance or biased decision-making—can erode public confidence in drug safety systems.(69)

Creating committees with experts from different fields, involving patients in decisions, and following ethical rules for using AI can improve accountability and transparency.

VI. FUTURE RESEARCH SCOPE IN PHARMACOVIGILANCE

Pharmacovigilance, the science of monitoring drug safety, has come a long way since the thalidomide crisis. However, as healthcare changes, new complex treatments emerge, and more real-world data becomes available, there's a need for ongoing improvements in how we monitor drug safety. The future of pharmacovigilance will likely include more active monitoring methods, using genetic information, involving patients more, advanced data analysis, and working together globally. A key area of research is developing systems to actively monitor drug safety after a drug is on the market. Traditional reporting systems are great for spotting potential issues but aren't as good at identifying individual patient risks or predicting how side effects might develop. Future research should focus on tools that can monitor over time and answer patient-focused questions, like whether a side effect will go away, how long it might last, and how best to manage it.(24)

Another promising area of research is pharmacogenetics and personalized medicine. Genetic predispositions significantly influence a person's vulnerability to adverse drug reactions (ADRs). By integrating pharmacogenomics with pharmacovigilance databases, we could facilitate the early identification of at-risk populations and support precision prescribing practices.(70) Advancements in biomarker discovery and genetic profiling will enhance risk prediction models, thereby empowering personalized therapeutic decision-making.

The rising engagement of patients offers a significant opportunity for research advancement. Today's healthcare landscape is shifting toward patient-cantered methods, transforming patients from passive recipients into active participants. The direct reporting of Adverse Drug Reactions (ADRs) through mobile applications, web-based intensive monitoring systems, and wearable technology enables the real-time gathering of safety data. Future studies should focus on assessing the validity, reliability, and incorporation of patient-reported outcomes into regulatory and clinical decision-making processes.(71) The emergence of big data and artificial intelligence (AI) presents a groundbreaking opportunity. Pharmacovigilance systems are progressively integrating electronic health records (EHRs), pharmacy information, hospital registries, and insurance claims alongside traditional approaches. Utilizing AI-driven algorithms, natural language processing, and machine learning can significantly improve signal detection, uncover hidden patterns, and deliver predictive safety analytics.(72)

The future of pharmacovigilance is moving away from reactive, harm-cantered methods and toward proactive, predictive, and patient-cantered systems. By integrating pharmacogenomics, digital health technologies, AI-driven analytics, and global collaboration, pharmacovigilance can advance into a more comprehensive scientific field, ultimately enhancing patient safety and therapeutic outcomes on a global scale.

VII. CONCLUSION ON THESE ARTICLE REVIEW

AI and machine learning are changing how we keep track of drug safety by offering new ways to solve old problems. Traditional methods, like waiting for reports from doctors or patients and keeping an eye out for issues, are still important but have problems like not enough reports, bias, and slow detection of rare or long-term side effects. AI and machine learning use tools like understanding language, predicting outcomes, and learning from data to quickly Analyse huge amounts of information, making it easier to spot safety issues accurately and on time.AI is great at gathering information from different places, such as report systems, health records, research papers, and social media, to get a better picture of drug safety. Automating standard tasks like taking in cases, finding duplicates, and sorting data reduces mistakes and boosts efficiency. Predictive models

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help by spotting high-risk patient groups, predicting drug interactions, and allowing for personalized safety checks. However, there are still challenges, like concerns about data privacy, bias in algorithms, and the need for transparency and responsibility. These must be managed with ethical guidelines, clear AI, and updated regulations. It's important to make sure AI systems are fair and inclusive to protect vulnerable groups. Overall, using AI and machine learning is turning drug safety monitoring from a system that reacts to problems into one that predicts and focuses on patients. By mixing tech innovation with ethical care, we can improve global drug safety and provide better healthcare for patients.

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