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Artificial Intelligence in Pharmacovigilance: Emerging Application for Enhanced Patient Safety

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Abstract: The goal of pharmacovigilance is to monitor, comprehend, and prevent adverse drug reactions (ADRs), unpleasant side effects, and other issues. From primarily manual adverse drug reaction (ADR) monitoring, pharmacovigilance has evolved into a technology-supported field that can handle sizable and intricate safety datasets. In order to find potential links between pharmaceuticals and adverse occurrences, data-mining and machine-learning approaches have been increasingly used to databases of spontaneous reports. Natural language processing (NLP) and more advanced machine-learning algorithms led to a significant expansion of artificial intelligence applications during the 2010s. To find trends in pharmacovigilance data and assist in the identification of possible drug-safety alerts, machine learning employs statistical and computational methods. A new method for forecasting adverse drug responses and other medication-related safety outcomes is machine-learning-based predictive modeling. AI-assisted risk assessment uses computer methods to identify and forecast possible safety issues related to pharmaceuticals. AI can find trends linked to adverse medication occurrences by analyzing data from pharmacovigilance databases, electronic health records, and other real-world data sources.

Keywords: *Pharmacovigilance, History, AI Basics, AI Technology, Machine Learning,*

INTRODUCTION

The goal of pharmacovigilance is to monitor, comprehend, and prevent adverse drug responses (ADRs), unfavorable side effects, and other issues [1]. However, pharmacovigilance now faces additional difficulties due to the increasing complexity of healthcare. Conventional safety monitoring mostly relies on professional manual review and spontaneous reporting methods. Despite their continued significance, these methods are losing their efficacy as the amount of clinical and pharmaceutical data keeps growing [2]. ADRs also put a significant strain on healthcare systems, accounting for about 5% of hospital admissions, higher medical costs, and worse patient outcomes [3]. Therefore, it's critical to improve the detection and reporting of ADRs. Machine learning (ML) and artificial intelligence (AI) have become viable methods for assisting this process. By automating the study of vast amounts of clinical data, these technologies can assist find potential adverse drug reactions (ADRs) more quickly and effectively. Clinical settings have also shown its value [4]. For example, studies that coupled an AI-based strategy with a trigger tool in an emergency room shown how these technologies could help detect adverse drug reactions (ADRs) and improve current medication-safety monitoring systems [5].

Manual data gathering and processing is challenging and time-consuming due to the growing quantity and variety of these data sources. Conventional methods may lead to duplicate entries in pharmacovigilance databases, under-recognition of adverse drug reactions (ADRs), and failure to detect possible drug-drug interactions (DDIs) [6,7]. These restrictions may ultimately compromise patient safety by decreasing the efficacy of medication safety monitoring [8]. Health-related data gathered outside of the controlled environment of clinical trials is referred to as "real-world data" (RWD). Electronic prescribing systems, insurance claims, patient registries, and electronic health records (EHRs) are a few examples. Because RWD can facilitate quicker and more efficient post-marketing drug safety monitoring, its usage in pharmacovigilance has grown in recent years [9].

Because it captures the real experiences of people and healthcare procedures throughout time, RWD is very helpful. As a result, it can offer useful data regarding medication safety in standard clinical settings. By discovering additional characteristics or confounding variables that may affect medication safety, analysis of RWD may also contribute to our current understanding of ADRs. Federated RWD networks, for instance, have recently been investigated to evaluate their utility in pharmacovigilance signal handling [10]. The early 2000s saw a rise in interest in the application of artificial intelligence (AI) in pharmacovigilance (PV), especially with the development of data-mining techniques for identifying safety signals in spontaneous reporting systems (SRS). The development of more sophisticated AI-based techniques in PV was greatly aided by techniques like the Multi-item Gamma Poisson Shrinker (MGPS) and the Bayesian Confidence Propagation Neural Network (BCPNN). AI has been incorporated into a number of PV tasks throughout time, such as automated case processing, safety signal recognition, and real-world evidence analysis [11,13].

HISTORY

From primarily manual adverse drug reaction (ADR) monitoring, pharmacovigilance has evolved into a technology-supported field that can handle sizable and intricate safety datasets. Following the thalidomide disaster, the necessity for rigorous drug-safety monitoring became more-clear. This led to the creation of international pharmacovigilance systems and established procedures for gathering and assessing suspected adverse drug reactions [14,15]. Computers were progressively included into drug-safety operations during the 1960s and 1970s, primarily for the storage, retrieval, and management of ADR reports. Although these early systems were not regarded as current AI, they laid the technological groundwork for later pharmacovigilance process automation [16].

Computerized databases, statistical methods, and early expert systems were increasingly investigated for pharmacovigilance in the 1980s and 1990s. These methods made it easier for safety experts to arrange a lot of information and spot odd trends that might indicate new safety issues [17]. A notable shift toward automated signal detection occurred in the 2000s. In order to find potential links between pharmaceuticals and adverse occurrences, data-mining and machine-learning approaches have been increasingly used to databases of spontaneous reports. Researchers were able to rank possible signals for additional clinical and regulatory evaluation using quantitative methods [18]. Natural language processing (NLP) and more advanced machine-learning algorithms led to a significant expansion of artificial intelligence applications during the 2010s. NLP made it possible to extract data from unstructured sources, such as clinical narratives, scholarly papers, and electronic health records. ADR identification, case classification, duplicate detection, literature screening, and safety-signal detection were all aided by these methods [19].

AI systems' capacity to identify intricate correlations in pharmacovigilance data has increased recently thanks to deep learning and transformer-based models [20]. Automated adverse-event extraction, drug-event link detection, literature monitoring, and other safety-related activities have all been studied using these technologies [21]. Pharmacovigilance now has more options thanks to the development of generative AI and large language models (LLMs) in the 2020s. Information extraction, case summaries, literature research, document creation, and other repetitious tasks may be aided by these systems [22]. However, if results are accepted without expert evaluation, there may be dangers due to inaccurate information, hallucinations, bias, privacy problems, and inadequate explainability [23].

Therefore, their application in drug safety requires comprehensive validation. If outputs are accepted without expert evaluation, hazards include information, hallucinations, bias, privacy problems, and inadequate explainability [24]. Numerous significant drug-related safety incidents have impacted the evolution of pharmacovigilance. Sulfanilamide elixir was linked to a significant poisoning occurrence in the US during the 1930s. Diethylene glycol was used as a solvent in the preparation, which led to 107 fatalities. The Federal Food, Drug, and Cosmetic Act of 1938, which tightened the procedures for proving drug safety prior to commercialization, was a result of this incidence [25].

The 1961 thalidomide disaster marked a significant turning point. Pregnancy-related thalidomide use was linked to severe congenital abnormalities, according to reports from doctors. The incident brought to light the shortcomings of pre-marketing safety evaluation and emphasized the significance of systematic reporting of adverse drug reactions and post-marketing drug monitoring. Pharmacovigilance systems and drug-safety laws underwent significant modifications as a result [26]. Diethylstilbestrol (DES), which was provided to expectant mothers, was another significant drug-safety incident. Subsequent research revealed detrimental long-term impacts in those exposed during pregnancy, indicating that certain negative effects might not show up for a long time. As a result, the DES experience highlighted the significance of post-marketing surveillance and long-term follow-up in medication safety [27].

In order to improve the tracking and reporting of adverse drug reactions (ADRs) and encourage the safe use of medications, the Ministry of Health and Family Welfare of India established the countrywide Pharmacovigilance Program of India (PvPI) in 2010. Since April 2011, the Indian Pharmacopeia Commission (IPC) has served as PvPI's National Coordination

Center (NCC). The program's network of Adverse Drug Reaction Monitoring Centers (AMCs) gathers and assesses ADR reports in order to support regulatory decision-making and identify any safety concerns. As a result, PvPI has been crucial in bolstering India's national pharmacovigilance system and enhancing medication safety [28].

Period	Technological Development	Application in Pharmacovigilance	References
1960s–1970s	Early computerized systems	Storage and management of ADR information	[29]
1980s–1990s	Expert systems and statistical methods	Support for ADR assessment and safety monitoring	[30]
2000s	Data mining and machine learning	Automated signal detection and identification of drug–event associations	[31]
2010s	NLP and advanced machine learning	Extraction of safety information from unstructured data	[32]
Late 2010s–2020s	Deep learning	Automated classification, prediction, and signal detection	[33]
2020s	Generative AI and LLMs (Large Language Models)	Summarization, information extraction, literature surveillance, and case-processing support	[34]

Table: 1. Historical Development of AI in Pharmacovigilance

AI Basics

AI/ML has the potential to affect PV and is being investigated over the whole lifecycle. Data ingestion-related tasks, signal detection activities, and other applications are the three broad categories into which ML in PV can be divided [35, 36].

1. Machine Learning (ML)

To find trends in pharmacovigilance data and assist in the identification of possible drug-safety alerts, machine learning employs statistical and computational methods. ML has been used in pharmacovigilance to detect adverse drug reactions, identify safety signals, predict risks, and analyze spontaneous reporting and large-scale healthcare data [37].

2. Deep Learning (DL)

Multi-layered neural networks are used in deep learning, an advanced type of machine learning, to find intricate patterns in big, diverse datasets. Deep learning techniques have been studied in pharmacovigilance to extract adverse medication events from clinical text, biological literature, social media, and other safety information sources [38].

3. Natural Language Processing (NLP)

Natural language processing, which is especially helpful for retrieving drug-safety information from unstructured text, allows computers to comprehend and interpret human language. NLP can be used in pharmacovigilance to extract drug-related safety information and adverse drug events from clinical text and other textual sources [39].

4. Computer Vision

Computer vision has potential uses in healthcare data analysis and allows computing systems to analyze and interpret visual data. Since its significance in pharmacovigilance is less well-established than that of ML, DL, and NLP, it might be regarded as an emerging field [40].

5. Expert Systems and Clinical Decision Support

To assist in the detection, assessment, and management of medication-related hazards, expert systems and clinical decision-support techniques integrate computational techniques with clinical expertise. AI-based methods in pharmacovigilance can help with real-world healthcare data analysis and drug safety evaluation [41].

AI TECHNOLOGIES

1. AI-Based Data Mining

One of the key computational techniques used in pharmacovigilance to find possible links between pharmaceuticals and adverse events from sizable safety datasets is data mining. Millions of drug-event combinations may be found in pharmacovigilance databases, making it challenging to manually assess every potential correlation. These datasets can be methodically screened and combinations that exhibit an extraordinary frequency of reporting can be prioritized using

computational data-mining techniques. Disproportionality-based techniques like the Reporting Odds Ratio (ROR), Proportional Reporting Ratio (PRR), Bayesian Confidence Propagation Neural Network (BCPNN), and empirical Bayes methods are frequently used. These techniques are mostly employed for signal generation and assist pharmacovigilance experts in identifying correlations that need more research [42].

Computational techniques are now used for purposes other than traditional statistical disproportionality analysis. Traditional statistical methods may be supplemented by machine-learning techniques, which may examine numerous variables and intricate patterns in safety data. Although conventional statistical techniques still predominate in the field, a scoping review of machine learning in pharmacovigilance found that signal detection was one of the most popular uses. This suggests that more recent computational techniques are presently employed mostly as supplementary instruments rather than as total substitutes for well-established pharmacovigilance techniques [43].

The fact that an observed statistical link does not always imply a causal relationship between a medication and an adverse occurrence is a significant drawback of data mining. Underreporting, stimulated reporting, missing data, duplicate reports, and confounding variables all have an impact on spontaneous-reporting databases. Therefore, rather than being verified adverse medication reactions, data-mining results should be considered as possible safety signals. Before making clinical or regulatory decisions, appropriate clinical evaluation and supplementary epidemiological data are necessary [44].

2. Automated Signal Detection

The process of automatically identifying and ranking possible drug-event connections from pharmacovigilance data is known as automated signal detection. When databases have a lot of reports, conventional signal detection may need a lot of manual evaluation. Large datasets can be quickly screened by automated computational techniques, which can also compute statistical metrics or predictive scores for drug-event pairings. This can assist pharmacovigilance teams in concentrating their efforts on relationships that are more likely to need in-depth evaluation [45].

Disproportionality analysis, Bayesian methods, temporal analysis, supervised machine learning, and other computational techniques have all been studied for automated signal detection. Instead of depending on a single signal-detection strategy, an integrated computational framework can mix several data sources and analysis techniques. This kind of integration could enhance the capacity to find complimentary evidence and make it easier to compare signals received through various techniques [46].

Predictive machine-learning algorithms for earlier signal recognition have also been studied recently. Gradient-boosting techniques, such as XG Boost, were examined in a pilot predictive-surveillance investigation to find possible safety signals, showing that predictive modeling can be added to traditional surveillance. Nevertheless, data quality, reporting bias, confounding, and shifts in reporting behavior can still have an impact on automated systems. Therefore, rather than determining whether a safety signal is clinically relevant on its own, computerized signal recognition should assist expert review [47].

3. Natural Language Processing for Literature Mining

Biomedical papers, clinical narratives, safety reports, product information, and patient-generated material are among the many unstructured textual sources of pharmacovigilance data. Computational techniques for deriving relevant safety information from such text are provided by Natural Language Processing (NLP). By identifying pharmacological names, adverse events, symptoms, diseases, and the connections between these things, natural language processing (NLP) transforms unstructured data into data that can be methodically examined [48]. NLP techniques may include named-entity identification, terminology normalization, relation extraction, text categorization, and information retrieval in biological literature and clinical narratives. These methods can help identify adverse medication occurrences and establish connections between pharmaceuticals and clinical results. The use of statistical and machine-learning techniques to extract adverse-event data from electronic health records and other textual sources has increased, according to reviews of NLP-based pharmacovigilance [49].

By examining social media posts where patients may discuss their experiences with medications in their native tongue, NLP can also aid in pharmacovigilance. Even though social media writing is frequently casual, condensed, unclear, and technically inconsistent, it might offer an additional source of possible adverse-event data. According to a comprehensive study, lexicon-based techniques and supervised classification have been widely employed for social media adverse-event identification; nonetheless, the lack of annotated datasets continues to be a significant obstacle. As a result, text mining and NLP-based literature should be viewed as supplementary methods to traditional pharmacovigilance data sources [50].

4. AI-Based ICSR Processing

Information about a specific patient who may have had an adverse event related to a medication is contained in an Individual Case Safety Report (ICSR). Case intake, pertinent information identification, validation, data input, coding, assessment, duplication detection, and follow-up are all typical steps in ICSR processing. Computational methods that can assist these operations and lessen tedious manual labor are required due to the growing number of safety reports [51]. Relevant information can be extracted from unstructured source documents and adverse-event narratives with the help of artificial intelligence and natural language processing. These tools are able to recognize and transform data into structured safety data, including clinical facts, adverse events, medication items, and patient characteristics. AI has been shown to have the ability to increase workflow efficiency in adverse-event case processing, freeing up pharmacovigilance specialists to concentrate on tasks requiring expert judgment [52].

ICSR prioritizing and triage can also be assisted by AI-based solutions. Reports can be categorized based on their probable relevance and requirement for case-by-case evaluation by combining NLP-derived data with structured factors. By selecting cases that need more attention and lowering the strain associated with normal case processing, these tools may assist pharmacovigilance teams in handling high volumes of reports [53]. Another significant use of AI in ICSR processing is duplicate detection. When the same adverse event is reported by many reporters or via different reporting channels, duplicate reports may result. To find reports that might describe the same clinical event, NLP can match data from case narratives and other report fields. Better deduplication can lower the likelihood of counting the same event more than once and improve the quality of pharmacovigilance databases [54].

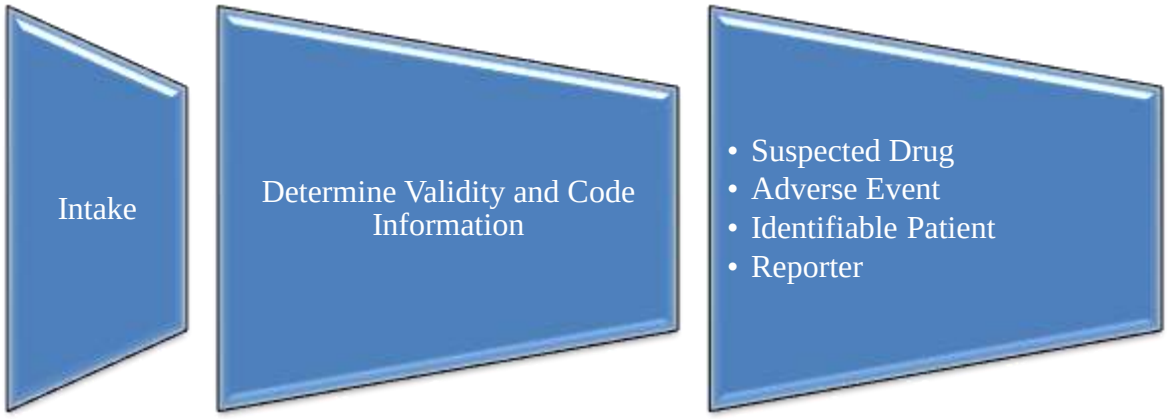


Figure: 1. Process Element Selected for Proof of Concept In AI-Based Adverse Event Case Processing [55].

5. Machine Learning-Based Predictive Modelling

A new method for forecasting adverse drug responses and other medication-related safety outcomes is machine-learning-based predictive modeling. Predictive modeling uses previously observed patterns to evaluate the likelihood of prospective safety outcomes, in contrast to classical signal detection, which primarily finds relationships already present in reported data. To find connections between pharmaceuticals, patient characteristics, and adverse events, machine-learning algorithms can examine past pharmacovigilance and clinical data [56]. For the purpose of predicting adverse medication reactions, various machine-learning techniques have been studied, such as decision trees, random forests, support vector machines, and deep learning models. These techniques can find intricate correlations in big datasets and investigate several factors at once. When adequate and well formatted data is available, deep learning techniques can further process high-dimensional data and perhaps produce helpful predictions [57].

Form: A Pilot, Predictive Surveillance Model in Pharmacovigilance Using Machine Leaning Approaches

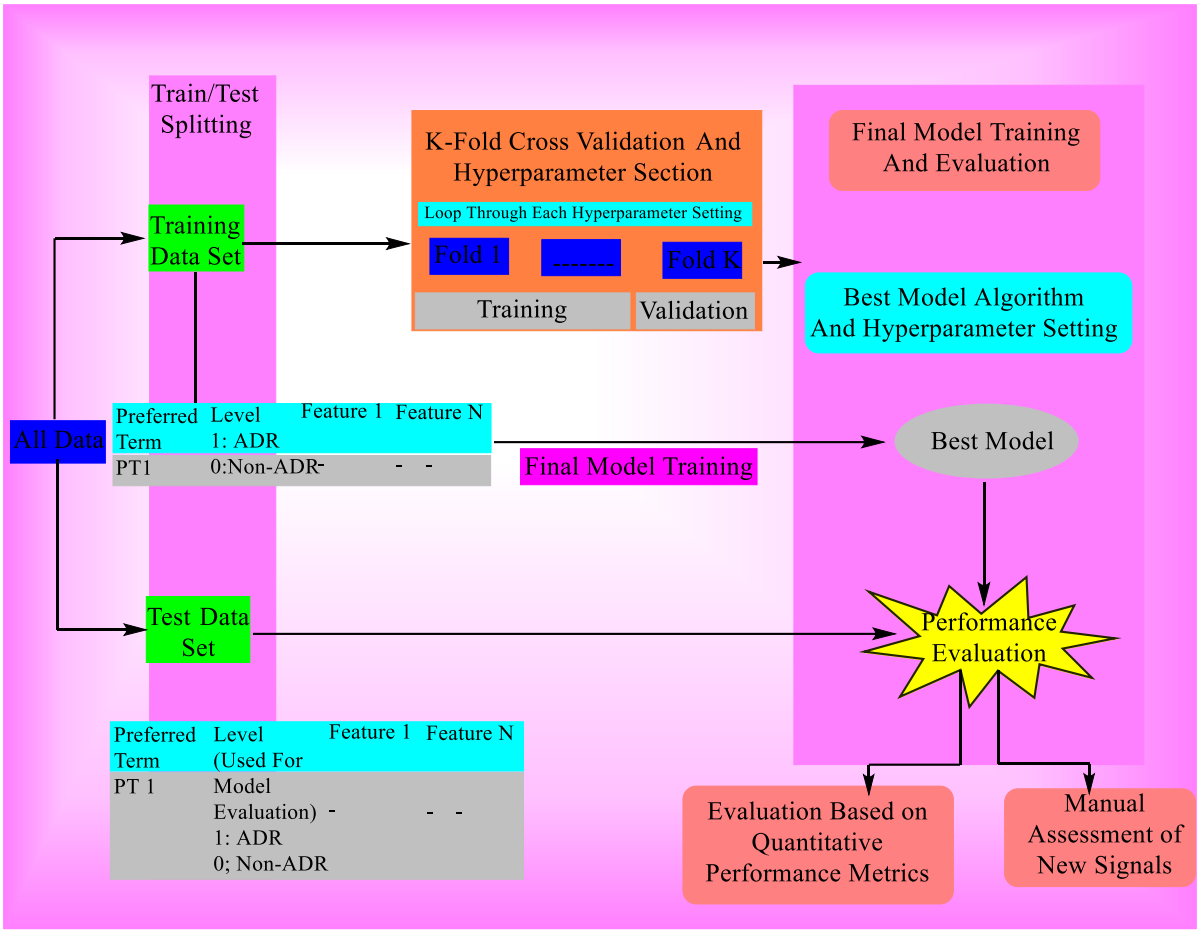


Figure: 2. Workflow of The Machine Learning Pipeline for Potential New Signal Detection [58].

By suggesting drug-event combinations that could need further research, predictive modeling can also assist prospective pharmacovigilance surveillance. Machine-learning methods are capable of continuously analyzing the safety data that is currently accessible and ranking possible hazards for additional assessment. However, representativeness, sample size, data quality, and validation techniques all have a significant impact on model performance. Therefore, before predictive models are included into standard pharmacovigilance practice, external validation and expert evaluation are crucial [59].

6. Knowledge Graphs

An organized depiction of the entities and connections found in biological data is offered by knowledge graphs. Knowledge graphs in pharmacovigilance can link pharmaceuticals to diseases, adverse medication reactions, genes, proteins, biological processes, and drug-drug interactions. Knowledge graphs might make it easier to integrate and analyze pharmacovigilance data from many sources by depicting these entities and their connections in an interconnected structure [60]. To anticipate possible negative medication effects, machine learning and deep learning techniques can be integrated with knowledge graphs. Instead of examining a medicine and an adverse event as a single pair, graph-based models can make use of interactions between several biological entities. In addition to offering more information for safety prediction, this interconnected model may aid in the identification of indirect or hitherto unidentified links [61].

Knowledge graphs are used in pharmacovigilance to predict adverse medication reactions, identify drug-drug interactions, and integrate heterogeneous safety data. Nonetheless, issues with data quality, interoperability, standardization, insufficient information, and validation of projected linkages still exist. The validity and usefulness of knowledge-graph-based techniques in pharmacovigilance and regulatory decision-making require more investigation [62].

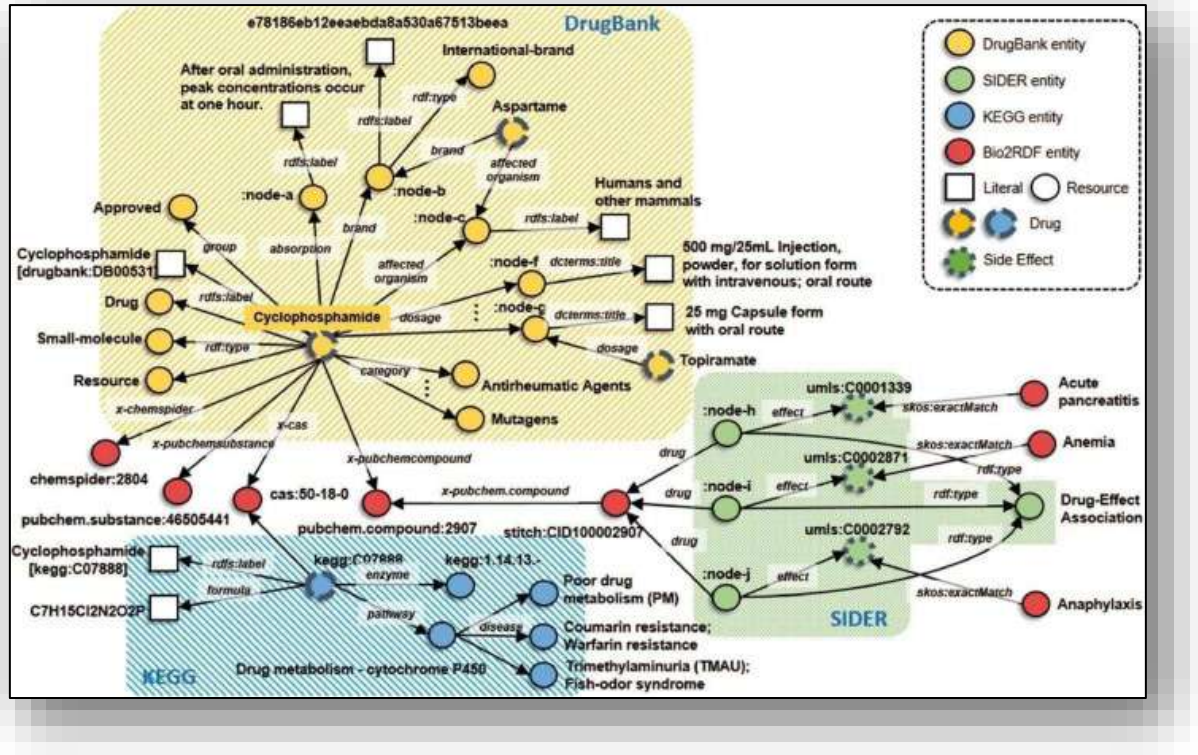


Figure: 3. Fragment of a Knowledge Graph Integrating Drug Bank, SIDER, and KEGG for the Drug Cyclophosphamide [63].

7. Generative AI and Large Language Models

Large Language Models (LLMs) and Generative Artificial Intelligence are two cutting-edge technologies that may find use in pharmacovigilance. These systems may help with tasks like literature screening, information extraction, summarization, translation, and safety narrative analysis. They can also handle and produce natural-language data. Pharmacovigilance workflows may become more efficient and less repetitive due to their capacity to handle massive amounts of textual data [64]. Additionally, LLMs have been studied for pharmacovigilance literature screening. The identification and selection of publications that might contain pertinent drug-safety information can be aided by their capacity to parse scientific content. Large language models can help with literature-screening tasks, according to comparative study, albeit how well they work depends on the model, the task's requirements, and the system's instructions [65]. The use of LLMs in pharmacovigilance necessitates the necessary precautions notwithstanding their potential advantages. Large language models may produce inconsistent outputs, unsupported claims, or erroneous information, which can be especially troublesome in situations when safety is crucial. Therefore, issues pertaining to hallucinations, transparency, reproducibility, and verification of generated information need to be carefully considered. Before LLMs are utilized for crucial pharmacovigilance decisions, human oversight and suitable validation are necessary [66].

8. AI-Assisted Risk Assessment

AI-assisted risk assessment uses computer methods to identify and forecast possible safety issues related to pharmaceuticals. AI can find trends linked to adverse medication occurrences by analyzing data from pharmacovigilance databases, electronic health records, and other real-world data sources. These methods may help identify high-risk medications, patient populations, or clinical scenarios and offer more data for benefit-risk analysis [67]. Because real-world data reflects medication use in typical healthcare settings, it can offer useful information for AI-assisted pharmacovigilance. To find possible safety trends, machine-learning models can examine patient characteristics, diagnoses, drug exposure, and clinical results. By offering more data from people and healthcare contexts that might not be adequately represented in conventional reporting databases, these methods could support spontaneous reporting systems [68].

AI can also help evaluate possible drug-drug interactions and dangers related to drug combinations. The early prediction and risk assessment of hazardous medication combinations have been studied using ensemble-learning techniques. These models could aid in the early detection of possible medication-related hazards and assist prioritize drug combinations that need additional clinical study [69]. However, before being used in clinical or regulatory practice, AI-assisted risk

assessment needs to be thoroughly examined. Data quality, bias, confounding, model validation, transparency, privacy, and human oversight are all crucial factors. A risk-based strategy, human oversight, validity and robustness, openness, data privacy, fairness, and accountability for responsible implementation are all highlighted in recent guidelines on AI in pharmacovigilance [70].

ADR DETECTION

A negative and unexpected reaction linked to the administration of a medication is known as an adverse drug reaction (ADR). Finding a potential link between a medication and an unfavorable clinical outcome is known as ADR detection. ADR detection can occur through several sources:

- Spontaneous adverse-event reports
- Electronic health records (EHRs)
- Hospital information systems
- Clinical notes
- Laboratory results
- Prescription databases
- Scientific literature
- Social media and online patient forums
- Clinical trials
- Patient registries
- Regulatory databases

Individual reports must often be reviewed by human professionals in order to identify traditional ADRs. When thousands or millions of reports are available, this method may take a long time. AI can help by automatically extracting pertinent facts from big datasets [73,75]. Take the following statement, for instance: "The patient developed severe dizziness three days after starting Drug X."

An NLP system may identify:

- Drug: Drug X
- Adverse event: dizziness
- Severity: severe
- Time relationship: three days
- Potential relationship: Drug X → dizziness

The extracted information can then be incorporated into a pharmacovigilance database and considered during signal detection.

1. Role of Natural Language Processing (NLP) in ADR Detection

One of the most significant AI tools for pharmacovigilance is natural language processing, or NLP. It enables computers to interpret human language found in patient-generated content, clinical notes, case reports, scientific papers, and medication labels.

Typically, NLP-based ADR detection entails:

1.1 Named Entity Recognition

Named Entity Recognition (NER) identifies important entities from text, such as:

- Drug names
- Adverse events
- Diseases
- Symptoms
- Laboratory abnormalities
- Patient characteristics
- Medical procedures

For example: “Patient developed acute kidney injury after administration of Drug A.”
The model can recognize:

Drug: Drug A
ADR: Acute kidney injury

Deep learning techniques can perform well in NER tasks for adverse drug event extraction, according to recent research [76].

1.2 Relation Extraction

After identifying entities, AI can determine relationships between them.

For example: Drug A → causes/suspected cause → acute kidney injury. Relation extraction is important because merely finding a drug and an adverse event in the same sentence does not necessarily mean that the drug caused the event.

1.3 Transformer and BERT Models

Transformer-based models like BERT (Bidirectional Encoder Representations from Transformers) are being used more and more in modern NLP. BERT-based methods performed well in end-to-end extraction tasks, according to research examining machine and deep learning approaches to clinical adverse drug event extraction [76].

Large language models (LLMs) may further assist with:

- Clinical text summarization
- ADR identification
- Case classification
- Literature screening
- Signal validation support
- Information extraction

However, because hallucination, inaccurate interpretation, and lack of explainability continue to be significant issues, LLM outputs need to be validated [77].

2. Role of Machine Learning for ADR Detection

From past pharmacovigilance data, machine learning algorithms can identify patterns that can be used to categorize or forecast possible adverse occurrences.

Common algorithms include:

- Logistic regression
- Decision trees
- Random forest
- Support vector machine (SVM)
- Naïve Bayes
- Gradient boosting
- XGBoost
- Artificial neural networks
- Convolutional neural networks
- Recurrent neural networks
- Transformer-based models

Machine learning has been used for a variety of PV activities, such as signal detection, data intake, real-world data analysis, and social media monitoring, according to a comprehensive review of ML applications in pharmacovigilance [73]. Random forests, logistic regression, and support vector machines were among the popular methods for exploratory pharmacovigilance utilizing electronic patient records, according to another review of machine learning employing big patient datasets [78].

3. AI-Based ADR Prediction

Predicting the likelihood of an adverse drug reaction (ADR) prior to or during treatment is another use for AI. Variables at the patient level could be:

- Age
- Sex
- Weight
- Medical history
- Comorbidities
- Laboratory values
- Previous medicines
- Concomitant medicines
- Dose
- Duration of treatment
- Genetic information, when available

For instance, a model might discover that patients with specific clinical traits are more likely to experience kidney damage after taking a specific medication. Studies utilizing laboratory data, comorbidities, and demographic variables were included in a recent systematic review of AI for predicting adverse drug reactions in hospitalized patients. Since many models have been built without adequate testing in independent populations, the review also emphasized the significance of external validation [79]. Therefore, clinical judgment should not be replaced by AI prediction. Alternatively, it can serve as a tool for risk categorization and decision assistance.

4. Signal Detection in Pharmacovigilance

Information indicating a new or altered link between a medication and an adverse event that needs more research is known as a safety signal. Crucially, a signal does not prove causation. The EMA expressly states that the existence of a safety signal does not prove that the medication was the cause of the reported adverse event; the incident could be explained by other medications, underlying medical conditions, or other causes [80].

The signal-management process includes:

Signal detection

↓

Signal validation

↓

Signal confirmation

↓

Signal analysis/prioritization

↓

Signal assessment

↓

Regulatory/action decision

These phases are referred to as formal signal management in the European regulatory framework [81].

5. Traditional Statistical Signal Detection

Statistical disproportionality techniques are used in traditional pharmacovigilance to find drug-event combinations that are reported more frequently than anticipated. Important methods include:

5.1. Reporting Odds Ratio (ROR)-

ROR contrasts the likelihood of reporting an adverse event for a specific medication with the likelihood of reporting the same event for other medications.

5.2. Proportional Reporting Ratio (PRR)-

PRR contrasts the percentage of reports pertaining to a certain event for a given medication with the same percentage for other medications.

5.3. Information Component (IC)-

The WHO-UMC technique to signal detection is linked to the Information Component, a Bayesian method utilized in the WHO pharmacovigilance system.

5.4. Empirical Bayes Methods-

Estimates can be stabilized with the use of empirical Bayes techniques, especially when low-frequency events are involved. These statistical methods are still quite significant. According to a recent scoping analysis, ML/DL methodologies accounted for a smaller percentage of reviewed pharmacovigilance studies than standard disproportionality methods like ROR and PRR [82].

6. AI and Machine Learning for Signal Detection

By spotting multidimensional and nonlinear patterns, AI can enhance conventional disproportionality analysis.

ML-based signal detection can incorporate:

- Drug characteristics
- Adverse event characteristics
- Patient factors
- Time-to-event relationships
- Concomitant medicines
- Laboratory data
- Clinical narratives

- Historical reporting patterns

For signal detection, models such random forest, gradient boosting, neural networks, and clustering algorithms have been studied [75,83]. ML techniques like random forest and gradient boosting have demonstrated potential for signal detection, while NLP has been especially helpful for signal validation and evaluation, according to a recent review of AI applications in pharmacovigilance signal handling [75]. AI's ability to prioritize thousands of drug-event pairings and assist pharmacovigilance specialists in concentrating on the most significant candidates is the main advantage.

7. AI-Based Signal Prioritization

Not every statistical signal indicates a safety issue that is clinically significant. As a result, signal priority is crucial. AI can rank signals according to factors such as:

- Number of reports
- Seriousness
- Fatal outcomes
- Novelty
- Reporting frequency
- Strength of association
- Patient vulnerability
- Biological plausibility
- Temporal relationship
- Previous evidence

Regulatory importance for example, an AI system may rank:
Drug A + mild headache → low priority
while:
Drug B + fatal liver failure → high priority

This aids investigators in determining which signal warrants immediate attention, but it does not establish that Drug B caused liver failure. Signal prioritizing, according to the EMA, is a procedure meant to find signals that could dramatically alter a medication's benefit-risk ratio or have a significant influence on patients or public health [81].

Major Data Sources for AI-Based Pharmacovigilance

1. FAERS (FDA Adverse Event Reporting System)

One significant US database for spontaneous reports is the FDA Adverse Event Reporting System (FAERS). It serves as a crucial source for post-marketing safety surveillance and includes reports of adverse events and medication errors that have been submitted to the FDA [84].
AI researchers can use FAERS to investigate:

- Drug–ADR associations
- Rare adverse events
- Safety signals
- Drug classes
- Patient characteristics
- Serious outcomes

2. VigiBase

A significant international database of individual case safety reports is VigiBase, which is kept up to date by the Uppsala Monitoring Center for the WHO Program for International Drug Monitoring. It is especially useful for identifying possible safety signals across nations and populations due to its global reach [85]. AI can be applied to VigiBase-related data for:

- Global signal detection
- Drug–event association analysis
- Rare-event identification
- Pattern recognition
- Signal prioritization

3. EudraVigilance

The European system for handling and evaluating possible drug-related adverse events is called EudraVigilance. It facilitates the electronic exchange of ICSRs and aids in the early identification and assessment of potential safety signals [86]. EudraVigilance is a significant source for suspected adverse reactions and safety signals, according to the EMA [80].

4. Electronic Health Records

EHRs contain information such as:

- Patient demographics
- Diagnoses
- Prescriptions
- Laboratory tests
- Clinical notes
- Hospital admissions
- Treatment outcomes

EHRs can offer longitudinal data about patients both before and after drug exposure, in contrast to spontaneous reporting. These massive datasets can be analyzed by ML to find potential ADRs and safety correlations [78,87].

5. Scientific Literature

Scientific literature is another important pharmacovigilance source.
Relevant information may be obtained from:

- PubMed
- MEDLINE
- Case reports
- Clinical studies
- Observational studies
- Systematic reviews

NLP can find possible drug-ADR correlations by screening a huge number of articles. The workload associated with manual literature surveillance may be lessened as a result.

SOCIAL MEDIA AND PATIENT-GENERATED DATA

Patients increasingly discuss medicine-related experiences on:

- Social-media platforms
- Online health forums
- Patient communities
- Drug-review websites

Early symptom information that has not yet been recorded in conventional reporting methods may be included in such data. According to a thorough assessment of NLP for user-generated content, NLP may enhance conventional pharmacovigilance by identifying ADR information from online textual content [72,88]. However, social-media data have important limitations:

- Unverified information
- Duplicate reports
- Lack of clinical details
- Uncertain drug exposure
- Incorrect terminology
- Selection bias

Therefore, social-media signals require confirmation using reliable clinical or regulatory sources.

AI- Based Analysis of Clinical Notes and Unstructured Data

AI's capacity to evaluate unstructured clinical data is one of its main advantages. Phrases like this may appear in clinical notes: "After beginning medication, the patient experienced nausea." or "After stopping the medication, the rash went away."

Because such data is written in natural language, traditional database analysis may have trouble analyzing it. The pertinent medication, event, treatment relationship, and result can all be extracted using NLP. Adverse drug event extraction from

clinical text and other sources can be supported by machine learning and deep learning, according to recent research that explicitly looked at AI-powered clinical text-based ADE detection [76].

Knowledge Graphs for Drug–ADR Relationships
Another emerging AI approach involves knowledge graphs.
A knowledge graph can represent relationships such as:

- Drug → associated with → ADR
- Drug → interacts with → Drug
- Patient condition → increases risk of → ADR

For example:
Drug A → hepatotoxicity → liver injury
Data from databases, clinical records, medicine labels, and scholarly articles can all be combined into the graph. AI can then produce hypotheses for more pharmacovigilance research and find missing or unexpected links.

Advantages of AI in Pharmacovigilance
The major advantages include:

- High-volume data processing
- Rapid ADR identification
- Automated literature screening
- Extraction of information from unstructured text
- Early identification of potential safety signals
- Signal prioritization
- Prediction of ADR risk
- Integration of multiple data sources
- Reduction of repetitive manual work
- Identification of complex relationships
- AI therefore has the potential to make pharmacovigilance more efficient and scalable [73,75].

Limitations and Challenges of AI in Pharmacovigilance
Despite its potential, AI-based pharmacovigilance has several limitations.

1. Data Quality
Pharmacovigilance data can contain:

- Missing information
- Duplicate reports
- Reporting bias
- Inconsistent terminology
- Incorrect drug names
- Incomplete clinical information

2. False Positives and False Negatives
AI may fail to detect a real safety issue or find a correlation that is not clinically significant.

3. Lack of Explainability
Certain deep-learning models operate as "black boxes," making it challenging for specialists to comprehend why a specific signal was given priority [89].

4. External Validation
It's possible that models created with one hospital or database won't work as well with another population. External validation is still a crucial prerequisite for developing generalizability, according to recent ADR-prediction research [79].

5. Privacy
Sensitive patient data can be found in clinical notes and EHRs. Thus, appropriate governance, anonymization, and data protection are required.

6. Human oversight

Signals produced by AI shouldn't always be regarded as verified ADRs. Professionals in pharmacovigilance are required to assess existing evidence, alternative interpretations, causality, and clinical relevance.

Future Prospective for Patient Safety

Rather of completely replacing pharmacovigilance specialists, the future of pharmacovigilance is probably going to entail a mixed human–AI model. A system in the future might incorporate:

FAERS + VigiBase + EudraVigilance + EHRs + Literature + Social media
↓

Data standardization

↓

NLP/LLM-based ADR extraction

↓

ML/DL-based relationship detection

↓

ROR/PRR/IC + AI signal detection

↓

AI-based signal prioritization

↓

Expert pharmacovigilance assessment

↓

Signal validation

↓
Regulatory action

While maintaining human clinical judgment, this integrated approach may increase the speed and scope of safety monitoring. Although AI technologies are becoming more widely available for various stages of signal management, methodological transparency, validation, explainability, and regulatory harmonization continue to be significant hurdles, according to recent studies [75,89,90].

CONCLUSION

This review article explains how AI is used in pharmacovigilance for patient safety, signal detection, ADR detection, and data sources. How AI will advance in the field of pharmacovigilance for patient safety in the future. These days, various methods are employed for medication development, drug design, and patient safety. Thus, we provide a fundamental understanding of this AI technique after reading this paper. It's time for pharmacovigilance to employ more conventional techniques like Bayesian, ROR, and PRR. PRR compares the percentage of reports involving a specific incident for a certain drug with the equivalent percentage for other medications, whereas ROR compares the chances of reporting an adverse event for a given drug with the odds of reporting the same occurrence for other drugs. AI can speed up and improve the efficiency of pharmacovigilance efforts by utilizing various data sources, including EHRs, spontaneous reports, scientific literature, and social media. With the potential to increase patient safety, artificial intelligence has emerged as a significant pharmacovigilance tool. It can aid in the early detection of adverse drug reactions (ADRs), the discovery of

safety signals, the analysis of massive data sets, and the forecasting of potential dangers associated with drugs. While AI has numerous advantages, it also has many drawbacks, such as low-quality data, underreporting of ADRs, data privacy concerns, bias, and the inability to comprehend how some AI models make choices. Therefore, human expertise should not be entirely replaced by AI. Rather, it ought to collaborate with experts in pharmacovigilance, who are able to decipher the findings and make the right safety choices.

REFERENCES

1. Jeetu G, Anusha G. Pharmacovigilance: a worldwide master key for drug safety monitoring. J Young Pharm. 2010;2(3):315–20.
2. Miguel A, Azevedo LF, Araújo M, et al. Frequency of adverse drug reactions in hospitalized patients: a systematic review and meta-analysis. Pharmacoepidemiol Drug Saf. 2012;21(11):1139–54.
3. E.C. Davies, C.F. Green, S. Taylor, P.R. Williamson, D.R. Mottram, M. Pirmohamed Adverse drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes PLoS One, 4 (2) (2009), Article e4439.
4. S.M. de Almeida, A. Romualdo, A. de Abreu Ferraresi, G.R. Zelezoglo, A.R. Marra, M.B. Edmond Use of a trigger tool to detect adverse drug reactions in an emergency department BMC Pharmacol Toxicol, 18 (1) (2017), pp. 1-7.
5. N. Falconer, M. Barras, N. Cottrell Systematic review of predictive risk models for adverse drug events in hospitalized patients Br J Clin Pharmacol, 84 (5) (2018), p. 846,
6. Hauben M: Artificial intelligence and data mining for the pharmacovigilance of drug-drug interactions. Clin Ther. 2023, 45:117-33. 10.1016/j.clinthera.2023.01.002
7. Kiguba R, Isabirye G, Mayengo J, et al.: Navigating duplication in pharmacovigilance databases: a scoping review. BMJ Open. 2024, 14: e081990. 10.1136/bmjopen-2023-081990.
8. Li R, Curtis K, Zaidi ST, Van C, Castelino R: A new paradigm in adverse drug reaction reporting: consolidating the evidence for an intervention to improve reporting. Expert Opin Drug Saf. 2022, 21:1193 204. 10.1080/14740338.2022.2118712
9. Patadia VK, Schuemie MJ, Coloma PM, Herings R, van der Lei J, Sturkenboom M, et al. Can electronic health records databases complement spontaneous reporting system databases? A historical-reconstruction of the association of Rofecoxib and acute Myocardial infarction. Front Pharmacol. 2018;9:594.
10. Gauffin O, Brand JS, Vidlin SH, Sartori D, Asikainen S, Català M, et al. Supporting pharmacovigilance signal validation and prioritization with analyses of routinely collected health data: lessons learned from an EHDEN network study. Drug Saf. Dec 07, 2023;46(12):1335-1352.
11. Hauben M and Hartford CG. Artificial intelligence in pharmacovigilance: scoping points to consider. Clin Ther 2021; 43(2): 372–379.
12. Salas M, Petracek J, Yalamanchili P, et al. The use of artificial intelligence in pharmacovigilance: a systematic review of the literature. Pharmaceut Med 2022; 36(5): 295–306.
13. Hauben M. Artificial intelligence and data mining for the pharmacovigilance of drug–drug interactions. Clin Ther 2023; 45(2): 117–133.
14. World Health Organization. The Importance of Pharmacovigilance: Safety Monitoring of Medicinal Products. Geneva: World Health Organization; 2002. 52 p.
15. World Health Organization. Safety Monitoring of Medicinal Products: Guidelines for Setting Up and Running a Pharmacovigilance Centre. Geneva: World Health Organization; 2000. 28 p.
16. Lindquist M. VigiBase, the WHO Global ICSR Database System: Basic Facts. Drug Information Journal. 2008;42(5):409–419.
17. van Puijenbroek EP, Bate A, Leufkens HGM, Lindquist M, Orre R, Egberts ACG. A comparison of measures of disproportionality for signal detection in spontaneous reporting systems for adverse drug reactions. Pharmacoepidemiology and Drug Safety. 2002;11(1):3–10.
18. Hauben M, Bate A. Decision support methods for the detection of adverse events in post-marketing data. Drug Discovery Today. 2009;14(7–8):343–357.
19. Bate A, Evans SJW. Quantitative signal detection using spontaneous ADR reporting. Pharmacoepidemiology and Drug Safety. 2009;18(6):427–436.
20. Harpaz R, DuMouchel W, Shah NH, Madigan D, Ryan P, Friedman C. Novel data-mining methodologies for adverse drug event discovery and analysis. Clinical Pharmacology & Therapeutics. 2012;91(6):1010–1021.
21. Harpaz R, DuMouchel W, Lependu P, Bauer-Mehren A, Ryan P, Shah NH. Performance of pharmacovigilance signal-detection algorithms for the FDA Adverse Event Reporting System. Clinical Pharmacology & Therapeutics. 2013;93(6):539–546.
22. Karimi S, Wang C, Metke-Jimenez A, Gaire R, Paris C. Text and data mining techniques in adverse drug reaction detection. ACM Computing Surveys. 2015;47(4):1–39.

23. Gurulingappa H, Fluck J, Hofmann-Apitius M, Toldo L. Identification of adverse drug event assertions in medical texts. Journal of Biomedical Semantics. 2012;3:15.
24. Gurulingappa H, Toldo L, Rajput AM, Kors JA, Taweel A, Tayrouz Y. Automatic detection of adverse events to predict drug label changes using text and data mining techniques. Pharmacoepidemiology and Drug Safety. 2013;22(11):1189–1194.
25. Beninger P. Pharmacovigilance: An Overview. Clin Ther. 2018;40(12):1991-2004. doi:10.1016/j.clinthera.2018.07.012.
26. Fornasier G, Francescon S, Leone R, Baldo P. An historical overview over pharmacovigilance. Int J Clin Pharm. 2018;40(4):744-747. doi:10.1007/s11096-018-0657-1.
27. Veurink M, Koster M, de Jong-van den Berg LTW. The history of DES, lessons to be learned. Pharm World Sci. 2005;27(3):139-143. doi:10.1007/s11096-005-3663-z.
28. Kalaiselvan V, Thota P, Singh GN. Pharmacovigilance Programme of India: Recent developments and future perspectives. Indian J Pharmacol. 2016;48(6):624-628. doi:10.4103/0253-7613.194855.
29. Lee CY, Chen YPP. Machine learning on adverse drug reactions for pharmacovigilance. Drug Discovery Today. 2019;24(7):1332–1343.
30. Cocos A, Fiks AG, Masino AJ. Deep learning for pharmacovigilance: recurrent neural network architectures for labeling adverse drug reactions in Twitter posts. Journal of the American Medical Informatics Association. 2017;24(4):813–821.
31. Jagannatha AN, Yu H. Bidirectional RNN for medical event detection in electronic health records. Proceedings of the Annual Meeting of the Association for Computational Linguistics. 2016:473–482.
32. Tatonetti NP, Fernald GH, Altman RB. A novel signal detection algorithm for identifying hidden drug–drug interactions in adverse event reports. Journal of the American Medical Informatics Association. 2012;19(1):79–85.
33. European Medicines Agency. Reflection Paper on the Use of Artificial Intelligence in the Lifecycle of Medicines. Amsterdam: European Medicines Agency; 2024.
34. U.S. Food and Drug Administration. Artificial Intelligence and Machine Learning (AI/ML) for Drug Development. Silver Spring, MD: U.S. Food and Drug Administration; 2024.
35. R. Ball, G. Dal Pan "Artificial Intelligence" for pharmacovigilance: ready for prime time? Drug Saf, 45 (2022), pp. 429-438
36. A. Bate, Y. Luo Artificial intelligence and machine learning for safe medicines Drug Saf, 45 (2022), pp. 403-405
37. Kompa B, Hakim JB, Palepu A, Kompa KG, Smith M, Bain PA, et al. Artificial intelligence based on machine learning in pharmacovigilance: a scoping review. Drug Saf. 2022;45(5):477-491. doi:10.1007/s40264-022-01176-1.
38. McMaster C, Chan J, Liew DFL, Su E, Frauman AG, Chapman WW, et al. Developing a deep learning natural language processing algorithm for automated reporting of adverse drug reactions. J Biomed Inform. 2023;137:104265. doi:10.1016/j.jbi.2022.104265.
39. Li Y, Tao W, Li Z, Sun Z, Li F, Fenton S, et al. Artificial intelligence-powered pharmacovigilance: a review of machine and deep learning in clinical text-based adverse drug event detection for benchmark datasets. J Biomed Inform. 2024;152:104621. doi:10.1016/j.jbi.2024.104621.
40. Artificial intelligence and big data for pharmacovigilance and patient safety. J Med Surg Public Health. 2024;3:100139. doi:10.1016/j.glmedi.2024.100139.
41. Dimitsaki S, Natsiavas P, Jaulent MC. Applying AI to structured real-world data for pharmacovigilance purposes: scoping review. J Med Internet Res. 2024;26:e57824. doi:10.2196/57824.
42. Harpaz R, DuMouchel W, Shah NH, Madigan D, Ryan P, Friedman C. Novel data-mining methodologies for adverse drug event discovery and analysis. Clin Pharmacol Ther. 2012;91(6):1010-1021. doi:10.1038/clpt.2012.50.
43. Kompa B, Hakim JB, Palepu A, Kompa KG, Smith M, Bain PA, et al. Artificial intelligence based on machine learning in pharmacovigilance: a scoping review. Drug Saf. 2022;45(5):477-491. doi:10.1007/s40264-022-01176-1.
44. Stephenson WP, Hauben M. Data mining for signals in spontaneous reporting databases: proceed with caution. Pharmacoepidemiol Drug Saf. 2007;16(4):359-365. doi:10.1002/pds.1323.
45. Hauben M. A brief primer on automated signal detection. Ann Pharmacother. 2003;37(7-8):1117-1123. doi:10.1345/aph.1C515.
46. Harpaz R, DuMouchel W, LePendu P, Bauer-Mehren A, Ryan P, Shah NH. Performance of pharmacovigilance signal-detection algorithms for the FDA adverse event reporting system. Clin Pharmacol Ther. 2013;93(6):539-546. doi:10.1038/clpt.2013.24.
47. Koutkias VG, Jaulent MC. Computational approaches for pharmacovigilance signal detection: toward integrated and semantically-enriched frameworks. Drug Saf. 2015;38(3):219-232. doi:10.1007/s40264-015-0278-8.

48. Harpaz R, Callahan A, Tamang S, Low Y, Odgers D, Finlayson S, et al. Text mining for adverse drug events: the promise, challenges, and state of the art. Drug Saf. 2014;37(10):777-790. doi:10.1007/s40264-014-0218-z.
49. Luo Y, Thompson WK, Herr TM, Zeng Z, Berendsen MA, Jonnalagadda SR, et al. Natural language processing for EHR-based pharmacovigilance: a structured review. Drug Saf. 2017;40(11):1075-1089. doi:10.1007/s40264-017-0558-6.
50. Sarker A, Ginn R, Nikfarjam A, O'Connor K, Smith K, Jayaraman S, et al. Utilizing social media data for pharmacovigilance: a review. J Biomed Inform. 2015;54:202-212. doi:10.1016/j.jbi.2015.02.004.
51. Schmider J, Kumar K, LaForest C, Swankoski B, Naim K, Caubel PM. Innovation in pharmacovigilance: use of artificial intelligence in adverse event case processing. Clin Pharmacol Ther. 2019;105(4):954-961. doi:10.1002/cpt.1255.
52. Bayer S, Clark C, Dang O, Aberdeen J, Brajovic S, Swank K, et al. ADE Eval: an evaluation of text processing systems for adverse event extraction from drug labels for pharmacovigilance. Drug Saf. 2021;44(1):83-94. doi:10.1007/s40264-020-00996-3.
53. Lieber T, Gosselt HR, Kools PC, Kruijssen OC, Van Lierop SNC, Härmark L, et al. Natural language processing for automated triage and prioritization of individual case safety reports for case-by-case assessment. Front Drug Saf Regul. 2023;3:1120135. doi:10.3389/fdsfr.2023.1120135.
54. Kreimeyer K, Dang O, Spiker J, Gish P, Weintraub J, Wu E, et al. Increased confidence in deduplication of drug safety reports with natural language processing of narratives at the US Food and Drug Administration. Front Drug Saf Regul. 2022;2:918897. doi:10.3389/fdsfr.2022.918897.
55. Schmider J, Kumar K, LaForest C, Swankoski B, Naim K, Caubel PM. Innovation in pharmacovigilance: use of artificial intelligence in adverse event case processing. Clin Pharmacol Ther. 2019;105(4):954-961. doi:10.1002/cpt.1255.
56. Lee CY, Chen YPP. Machine learning on adverse drug reactions for pharmacovigilance. Drug Discov Today. 2019;24(7):1332-1343. doi:10.1016/j.drudis.2019.03.003.
57. Lee CY, Chen YPP. Prediction of drug adverse events using deep learning in pharmaceutical discovery. Brief Bioinform. 2021;22(2):1884-1901. doi:10.1093/bib/bbaa040.
58. De Abreu Ferreira R, Zhong S, Moureaud C, Le MT, Rothstein A, Li X, Wang L, Patwardhan M. A pilot, predictive surveillance model in pharmacovigilance using machine learning approaches. Adv Ther. 2024;41(6):2435-2445. doi:10.1007/s12325-024-02870-5.
59. Dimitsaki S, Natsiavas P, Jaulent MC. Applying AI to structured real-world data for pharmacovigilance purposes: scoping review. J Med Internet Res. 2024;26:e57824. doi:10.2196/57824.
60. Hauben M, Rafi M, Abdelaziz I, Hassanzadeh O. Knowledge graphs in pharmacovigilance: a scoping review. Clin Ther. 2024;46(7):544-554. doi:10.1016/j.clinthera.2024.06.003.
61. Joshi P, Masilamani V, Mukherjee A. A knowledge graph embedding based approach to predict the adverse drug reactions using a deep neural network. J Biomed Inform. 2022;132:104122. doi:10.1016/j.jbi.2022.104122.
62. Wang H, et al. Prediction of adverse drug reactions based on knowledge graph embedding. BMC Med Inform Decis Mak. 2021;21:38. doi:10.1186/s12911-021-01402-3.
63. Hauben M, Rafi M. Knowledge graphs in pharmacovigilance: a step-by-step guide. Clin Ther. 2024;46(7):538-543. doi:10.1016/j.clinthera.2024.03.006
64. Mishra HP, Gupta R. Leveraging generative AI for drug safety and pharmacovigilance. Curr Rev Clin Exp Pharmacol. 2025;20(2):89-97. doi:10.2174/0127724328311400240823062829.
65. Li D, Wu L, Zhang M, Shpyleva S, Lin YC, Huang HY, et al. Assessing the performance of large language models in literature screening for pharmacovigilance: a comparative study. Front Drug Saf Regul. 2024;4:1379260. doi:10.3389/fdsfr.2024.1379260.
66. Hakim JB, Painter JL, Ramcharran D, Kara V, Powell G, Sobczak P, et al. The need for guardrails with large language models in pharmacovigilance and other medical safety critical settings. Sci Rep. 2025;15:27886. doi:10.1038/s41598-025-09138-0.
67. Bate A, Hobbiger SF. Artificial intelligence, real-world automation and the safety of medicines. Drug Saf. 2021;44(2):125-132. doi:10.1007/s40264-020-01001-7.
68. Crisafulli S, Ciccimarra F, Bellitto C, Carollo M, Carrara E, Stagi L, et al. Artificial intelligence for optimizing benefits and minimizing risks of pharmacological therapies: challenges and opportunities. Front Drug Saf Regul. 2024;4:1356405. doi:10.3389/fdsfr.2024.1356405.
69. Prejesh S, Murugan TK, Govindaraj L. Early prediction and risk assessment of adverse drug combinations using ensemble learning. Sci Rep. 2026. doi:10.1038/s41598-026-58932-x.
70. Norén GN, Durand J, Kara V, et al. Artificial intelligence in pharmacovigilance: guiding principles from the CIOMS Working Group XIV. Drug Saf. 2026. doi:10.1007/s40264-026-01708-z.
71. World Health Organization. Pharmacovigilance: Ensuring the Safe Use of Medicines. WHO Policy Perspectives on Medicines. Geneva: WHO; 2004.

72. Beninger P. Pharmacovigilance: an overview. Clinical Therapeutics. 2018;40(12):1991–2004.
73. Kompa B, Hakim JB, Palepu A, et al. Artificial intelligence based on machine learning in pharmacovigilance: a scoping review. Drug Safety. 2022;45:477–491.
74. Pilipiec P, Liwicki M, Bota A. Using machine learning for pharmacovigilance: a systematic review. Pharmaceutics. 2022;14(2):266.
75. Warner J, Prada Jardim A, Albera C. Artificial intelligence: applications in pharmacovigilance signal management. Pharmaceutical Medicine. 2025;39:183–198.
76. Li Y, Tao W, Li Z, et al. Artificial intelligence-powered pharmacovigilance: a review of machine and deep learning in clinical text-based adverse drug event detection for benchmark datasets. Journal of Biomedical Informatics. 2024;152:104621.
77. Artificial intelligence and large language models in pharmacovigilance: emerging applications and challenges. Recent literature highlights concerns regarding hallucination, validation and explainability.
78. Exploratory pharmacovigilance with machine learning in big patient data: a focused scoping review. Clinical Epidemiology. 2022.
79. Artificial intelligence (AI) in pharmacovigilance: a systematic review on predicting adverse drug reactions in hospitalized patients. 2025.
80. European Medicines Agency. Signal Management. EMA.
81. European Medicines Agency. Guideline on Good Pharmacovigilance Practices (GVP), Module IX – Signal Management. EMA.
82. Data mining methods, tasks, and algorithms for adverse drug reaction analysis in pharmacovigilance: a scoping review. International Journal of Medical Informatics. 2026.
83. Machine learning approaches for pharmacovigilance signal detection and evaluation. Recent studies have investigated random forest, gradient boosting, neural networks and clustering methods for safety-signal identification.
84. U.S. Food and Drug Administration. FDA Adverse Event Reporting System (FAERS) Database. FDA.
85. Uppsala Monitoring Centre. VigiBase: WHO Global Database of Individual Case Safety Reports. UMC/WHO Programme for International Drug Monitoring.
86. European Medicines Agency. EudraVigilance. EMA. The system supports electronic exchange of ICSRs and early detection and evaluation of possible safety signals.
87. Coste A, et al. Methods for drug safety signal detection using routinely collected observational electronic health care data: a systematic review. Pharmacoepidemiology and Drug Safety. 2022.
88. NLP and machine learning for pharmacovigilance using user-generated content: a systematic review. Evidence indicates that NLP can complement conventional PV by extracting ADR information from internet-based patient-generated text.
89. Beyond black boxes: using explainable causal artificial intelligence to separate signal from **noise in pharmacovigilance. International Journal of Clinical Pharmacy. 2025.**
90. Barbieri MA, Battini V, Carnovale C, et al. Artificial intelligence in pharmacovigilance signal management: a review of tools, implementations, research, and regulatory landscape. Expert Opinion on Drug Safety. 2026;25(2):207–222.