



# ARTIFICIAL INTELLIGENCE-BASED PHARMACOVIGILANCE- A REVIEW

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## Abstract

For pharmacovigilance, automation has the promise of being a game-changer by lowering the cost of case reporting and enhancing data quality to genuinely offer value, including signal detection in drug safety. Analytical and benefit-risk analysis in pharmacovigilance. The evolution of pharmaceutical PV strategy is significantly influenced by technological advancements. For example, more businesses are recognising the need of big data analytics, cloud-based solutions, mobile apps, robotic automation, and artificial intelligence in the pharmaceutical industry's clinical safety and regulatory processes. In order to effectively manage the safety of pharmaceutical goods, it is increasingly essential to implement cutting-edge technological automation tools and procedures to PV methods. Artificial intelligence and machine learning can increase productivity in the identification, detection, management, and reporting of ADRs in pharmacovigilance. The primary goal of artificial intelligence is to solve problems that cannot be solved automatically, such as obtaining the right training data for machine learning models and the requirement for unified regulatory guidelines. Fast-moving AI that never gets tired or ill can analyse and comprehend data at breakneck speeds. The ICSR in PV, which includes native automation and stand-alone technologies like AI and ML that decrease the manual labour, processes thousands of adverse impacts each month.

**Keywords** – Automation, Health care system, Automation in Pharmacovigilance, Machine Learning [ML], Artificial Learning [AI].

## Introduction

Pharmacovigilance: The Etymological roots for the word “Pharmacovigilance” are Pharmacon (Greek) = medicinal substance, and Vigilance (Latin) = to keep watch.[1]

In accordance with the WHO, pharmacovigilance (PV) is the science and actions relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems. Adverse drug reactions are reported world in a variety of languages and formats, as well as in organised, unorganized, and handwritten documents; on average, several businesses get more than 3 lakh ADRs annually. With manual processes, human mistake is possible, and the whole project cost eventually increases. It is possible to apply AI-based technology to enable case validity assessment and extraction from AE source documents. Automation is the process of carrying out tasks or eliminating tasks with the aid of technology, hence minimising human dependency. Many government health authorities participate in pharmacovigilance activities on a daily or irregular basis. Machine learning (ML) and artificial intelligence (AI), as described by Lewis and McCallum, have begun to alter how safety and pharmacovigilance (PV) experts handle and interpret data to support decision making.[1,18,19]

## Tools and software's in AI

Artificial intelligence technologies in pharmacovigilance are the very helpful in determining the exact information about the case study, safety reporting etc. Artificial intelligence tools helps automation and in facilitating the almost every aspect of Pharmacovigilance in risk tracking, case processing, which reduces the total processing time.[7] .....**Following are some tools which are useful in PV activities:**

### vigibase

- it helps in recording the data in a structured and ordered form(1)

### vigi access

- it helps in accessing the data of adverse drug effects through vigibase

### vigilyze

- it helps in the quick review of vigibase(2)

### vigiFlow

- it helps in ICSR management system for international drug monitoring(3)

### vigi Grade

- it is used as an communicator among countries for data quality(4)

### vigiMatch

- it helps in detection of similar case by using prababilistic pattern matching.(5)

### vigiRank

- it is a novel method to detect the statistical signals(6)

## Need of artificial intelligence

PV was designed and implemented to strengthen the patient safety who are exposed to various drugs during clinical trials for a prolonged period of time, which includes different groups such as geriatric population, paediatric population, racial groups and pregnant women. [8]

PV performs the assessment, communication for risk and effectiveness of various life-saving drugs such as antitubercular, antiretroviral and anticancer drugs..etc based on fast track system.

In many countries, PV is still a new branch of science with less importance. Worldwide the countries are raising the issues in concern for the need of systems to monitor the safety of drug post marketing.[9] Reporting of adverse drug reaction (ADR) is mainly done through spontaneous reporting or by pharmacoepidemiological methods that use systematic collection and analysis of adverse events (AE) associated with the use of drugs. It is also done by Adverse Drug Reaction Monitoring Centres and marketing authorization holder (MAH) industries to solve emerging problems, record signals, and communicate to minimize or prevent harm.

The challenging operations of PV are coding of AE in technical terms, detection and reporting of ADRs, assessment of seriousness, preparing safety individual reports, and relationship with suspected drug. All these operations specially reporting of ADRs are time consuming and was in a need of new and upgraded technology. Thus a new technology with a named artificial intelligence was discovered with the collaboration of pharmaceutical industry and professional services to facilitate the maintenance and processing of quality and compliance standards.AI helps in tracking the globally available data easily which was quite difficult by the other available methods. AI techniques play a significant role in the area of drug design and identification of AEs of pharmaceutical products.[10]

## Applications of AI in PV

### 1. Regulatory

AI has been started and used in various fields of PV but is not mature enough for vast implementation. The COVID-19 pandemic demonstrated the importance of an agile, rapid approach as new medications were fast-tracked through the FDA's new regulatory pathways.

Even pre-pandemic, the FDA released a 5-year plan for integrating AI into the co-existing PV framework.(11)

### 2. Clinical

For a drug to be get approved and enter into te market it takes about 10-12 years of time including 5-6 years of clinical trial period. During clinical trials, some operations such as patient recruitment and site selection are time consuming and often leads to trial failure due to many circumstances.

Thus pharmaceutical companies are looking forward for new technology like AI to reduce the research and development cost, to examine a large number of cases and assist the personalizing data (12)

## Forms of AI

### Machine Learning

AI allows the software to learn and study the machine over a time without following the explicit instructions and improves from previous data to enhance its behavior and create new predictions.[13]

### Supervised Learning

In this algorithms are used to predict appropriately which label corresponds to an individual component. Thus the input of AI are labelled with the corresponding output. (14)

### Unsupervised Learning

It is basically machine learning type in which algorithms are used to analyse the unlabeled data 17 Although the model is using unlabeled data, it looks for recurring patterns that exist within the input data.[15]

### Semi-supervised Learning

It is the combination of unsupervised and supervised learning. Here, labeled data are combined with unlabeled data to earn the predict models better. Semi-supervised learning algorithms are used when the data is incomplete.[15]

### Reinforcement Learning

It is used when prior experiences are used to make adequate decisions. The prior experience helps in improving the algorithms with the help of constant feedbacks. 16 AE can be prevented by focusing on specific traits.[15]

## Current role of AI in healthcare

The most massive impact of artificial intelligence and machine learning is in continuous learning repeated data-rich tasks, with clarity on a successful outcome, see for example. With the use of health data and a retrospective ML analysis of mammography pictures, IBM and colleagues were able to predict biopsy-proven cancer and distinguish between normal and poor screening exams. According to the scientists, their algorithm may evaluate breast cancer at a level "equivalent with radiologists" and might significantly reduce the amount of missed breast cancer diagnosis.[16] Predicting asthma attacks is another example of using AI in healthcare, mobile applications for insulin monitoring, identifying the osteoporosis risk groups, monitoring the progress of anticoagulant therapy compliance, control of TB [Tuberculosis]. Recurrent neural networks additionally serve to produce voice acoustics by decoding brain activity, and machine learning is used to more efficiently identify and possibly enrol people in prospective research, such as randomised clinical trials. Together, these illustrations highlight the scope of developments in healthcare overall made possible by AI/ML. The same broad requirements and potential possibilities exist in safety, and new insights into illness and its course as well as healthcare delivery are made possible.[17]

## Impact of AI

Toxicology and the knowledge of safety in early pre-clinical drug development are two areas where significant ML is being studied, e.g. however in this instance, our attention is on human safety. Although we may have seen less automation and AI/ML in PV than in some other industries, it would be incorrect to think that these techniques are brand-new to the industry. For example, Neural networks were trained early in the 1990s to distinguish between tricyclic antidepressants and selective serotonin reuptake inhibitors based on side-effect patterns. More recently, the concept of using ML to make PV more profitable as data volumes increased was a major driver for the now-common usage of quantitative signal detection techniques.[17,18]

## Current challenges

The early published PV research reveals that AI/ML algorithms function well but not flawlessly, therefore there is still a barrier in how this would transfer into practical utility on a daily basis.[19]

The importance of pharmacovigilance in healthcare is crucial and critical. The application of artificial intelligence (AI) in this industry, however, is still a young and emerging sector. The availability of organised and curated data for training the programme to detect possible medication safety hazards is one of the big hurdles to using AI. Additionally, there are privacy issues with employing AI for pharmacovigilance because data might perhaps be utilised for other reasons without the agreement of those concerned.[19,22]

Human expert techniques for ICSR causality evaluation employ data from both inside and outside the report. To further the use of AI to ICSR processing and assessment, a well-defined "cognitive framework" that can be made computable and fit into current workflows must be developed. Case-series assessments and statistical disproportionality studies are now mostly independent processes. In order to more precisely discover odd patterns in case series, it may be possible to combine conventional statistical approaches with NLP and ML algorithms by developing a computable cognitive framework.[20, 25]

A related issue is that, historically, clinical disciplines have been the main source of recruitment for PV professionals, who have had little formal training in quantitative and computational methods of data processing. The effective adoption of AI systems for PV will depend on the education of PV personnel who are not AI specialists and the targeted hiring of AI professionals to assist AI applications for PV. This is true for both industry and regulatory organisations[19,20].

## AI for ICSR Processing

- A. Efficiency in decision-making - In some situations, the quality of the data in an INDIVIDUAL CASE SAFETY REPORT is subpar. In these situations, artificial intelligence is essential for developing hypotheses. Accuracy and speed of the content might be enhanced by artificial intelligence
- B. The components for reading incoming case intake information through XML, documentation, pictures including PDF and PDF text comprising forms and tables make up the ingestion of structured and unstructured content. Here, ICSR information is extracted from information sources using OCR/ICR, NLP, and machine learning in a way that complies with regulations.[20,21]

A lot of the challenges experienced by PV experts might be resolved by automation.

## Importance of AI and Automation in pharmacovigilance

The use of AI and automation in pharmacovigilance procedures can help with the detection of signals, monitoring, risk management, intake of AEs, and the creation of reports.[21,26]

Signal detection and automated case processing: Automation can aid in case processing at several stages of the procedure. With NLP (natural language processing), an automated system may comprehend both structured and unstructured data from a variety of different sources. Finding duplicates, analyzing data to look for terms or patterns that point to major patient risks or unidentified AEs, and reporting data after review are all steps in the process.[22,27]

Another area where AI and automation can significantly enhance is post-marketing surveillance (PMS), or monitoring medication safety after a product has hit the market. Mainly because of the enormous real-world datasets that may be combined at this point, ranging from active monitoring to scholarly literature and case reports.[22,23]

## Advantages

- Machine learning[ML]- Unsupervised learning has no ground truth and is utilised for signal management, but supervised learning used in PV for ICSR processing may train ML algorithms where ground truth, i.e., Human annotated response file.[30]
- Semantic search - improve the comprehension of searchers.
- Optical character recognition (OCR) - detect text in scanned documents, as well as for handwritten text verification.
- Chabot's - NLP may be used to perform human conversation using text or voice methods.
- Text analysis - investigate gathered data from sources into evidence by structuring unstructured text.
- Sentiment analysis - in the sense of text extraction from context[24,28]

## Disadvantages

- Investment costs. The cost of implementing a process automation system is high at first.
- Loss of adaptability. Change workflows; some jobs and procedures may be stiff.[24,29]

## Conclusion

Automation in the pharmacovigilance industry can increase workflow process efficiency, resulting in less effort and time. This customised method will be used using the traditional paper method, enhancing clinical decision-making. This difficult method converts data and concurrently transmits information to various recipients since risk minimization is always the first priority.

Information on centralised adverse event reports from any location in the globe is available through cloud-based integrated global ADR repository reporting. The use of social media and smartphone applications has become widespread, providing an open forum for anybody to report and gather AE data. In the future, mobile applications might take the role of patient information booklets, package inserts, and prescription guidelines. Future pharmacovigilance procedures will be dominated by the use of digitalized medications with ingestible sensors to follow and gather patient health data, including AE detection.

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