Transformation in Pharmacovigilance Signal Detection: From Spontaneous Reporting System to Artificial Intelligence Integration

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Abstract

Adverse drug reactions (ADRs) are a global health problem that has a significant impact on patient safety and healthcare system efficiency. Spontaneous reporting systems (SRS) have been the main approach in pharmacovigilance signal detection, but still face obstacles such as underreporting, reporting delays, and reporter bias. Meanwhile, the development of artificial intelligence (AI) offers transformational potential through big data-based automated ADR detection. This review aims to comprehensively evaluate the differences and potential integration between SRS and AI in pharmacovigilance signal detection. The method used was a narrative review of original literature published between 2015-2025 from PubMed, BMC, and Google Scholar databases. A total of 63 articles were screened, and 11 key studies were analyzed in depth. Results showed that although various interventions were able to improve ADR reporting through SRS, their effectiveness was limited. In contrast, AI demonstrated high capability in detecting ADRs from unstructured data with superior accuracy and speed. In-depth discussions highlighted that AI approaches can strengthen pharmacovigilance systems that have relied on manual reporting. In conclusion, the integration of SRS and AI is a promising strategy to address modern pharmacovigilance challenges, and should be adopted through a national system supported by regulation, data digitization, and human resource capacity strengthening.

Keywords: pharmacovigilance, adverse drug reactions, spontaneous reporting system, artificial intelligence

1. INTRODUCTION

Pharmacovigilance (PV) is a scientific and regulatory activity related to the detection, assessment, understanding, and prevention of adverse drug events or other problems associated with drug use. Pharmacovigilance can help in detecting new or unknown signals between drugs and adverse reactions. Adverse drug reactions (ADRs) are a public health problem that requires the attention of all stakeholders regardless of the practice environment (Ampadu et al., 2016).

The incidence of ADRs in the world represents a significant burden to the global health system. In high-resource countries, ADR reporting reaches between 3 - 613 reports per one million population per year (Aagaard et al., 2012). Developing countries show wide variations in reporting, ranging from zero to 50,000 ADR reports per year. Thailand, Malaysia and Singapore have the highest reporting rates in the Southeast Asian region. Patient self-reporting of ADRs is still very low, with the highest rate recorded in Denmark

(467 reports per million population), while in Asian countries such as Malaysia and the Philippines it only reached 0.86 and 0.01 reports per million population (Worakunphanich et al., 2022). Globally, more than 43,000 reports of ADR deaths were recorded in the WHO-VigiBase database during the period 2010 to 2019 (Montastruc et al., 2021). These data confirm that ADRs pose a serious threat to patient safety and healthcare efficiency worldwide.

Healthcare workers are the focal point in operationalizing a pharmacovigilance system capable of managing ADRs (Güner & Ekmekci, 2019). With insufficient knowledge, health workers may not be able to report ADRs appropriately (De Angelis et al., 2016). However, they are required to have a good understanding and skills in the area of drug safety related to detecting, recognizing, managing and reporting suspected adverse drug reactions (van Eekeren et al., 2018). SRS have long been used as a traditional method of detecting pharmacovigilance signals (WHO, 2002). However, as information technology develops, AI methods are being used to improve the efficiency and accuracy of signal detection (Warner et al., 2025).

The development of AI technology opens up opportunities to strengthen PV systems through automatic detection and analysis of unstructured data. Unfortunately, to date, there are not many studies that systematically compare the strengths and limitations of each SRS and AI approach, especially in the context of integration for national systems. Therefore, this study aims to critically analyze the differences and potential synergies between SRS and AI in pharmacovigilance signal detection, and evaluate their relevance to the challenges of PV implementation in the digital era.

2. METHOD

This review is a narrative review of the literature organized following the PRISMA guidelines for narrative reviews. Literature was searched through online databases such as PubMed, BMC, and Google Scholar using the keywords: *"adverse drug reactions", "pharmacovigilance", "signal detection", "spontaneous reporting system", "artificial intelligence", and "machine learning"*. Inclusion criteria included original articles, in English, published between 2015 and 2025 and relevant to ADR signal detection via SRS or AI.

From a total of 147 articles found, 63 articles met the inclusion criteria after screening based on title, abstract, and full text. A total of 11 key studies were reviewed in depth as they specifically compared or addressed the effectiveness and challenges of ADR reporting through SRS and AI. Data were analyzed and presented in a descriptive-comparative manner.

3. RESULTS AND DISCUSSION

According to the results of a study conducted by that SRS faces challenges in timeliness and data completeness, so the application of AI models successfully identified more potential ADR cases although it still requires expert judgment at the clinical validation stage to interpret the results (Crisafulli et al., 2025). As technology develops, AI integration is being applied to overcome these shortcomings and improve signal detection more quickly and accurately. The results of studies related to the development of ADR detection systems from conventional methods to the utilization of AI are presented in Table 1 below.

Table 1. ADR Pharmacovigilance Studies on SRS and AI

No.	Author	Title	Result
1.	Asiamah et al. (2022)	Spontaneous reporting of adverse drug reactions among health professionals in Ghana	1. Factors that significantly influenced spontaneous ADR reporting were age (AOR = 2.26), pharmacovigilance training (AOR = 18.78), and barriers such as legal fear (AOR = 0.15), time constraints (AOR = 0.3), and unavailability of reporting forms (AOR = 0.28). 2. The proportion of spontaneous reporting of ADRs by health workers in Kpone-Katamanso District is low, thus requiring a mandatory reporting policy for health workers.
2.	Fang et al. (2017)	Multifaceted interventions for improving spontaneous reporting of adverse drug reactions in a general hospital in China	1. Physician training, KAP education, and economic incentives improved SRS compliance, while changes in drug guidelines affected ADR patterns and types. 2. SRS adherence improved through multifaceted interventions. 3. Drug use patterns affect ADRs, so rational use programs are important to strengthen SRS and pharmacovigilance development in China.
3.	Yu & Lee, (2017)	Enhanced knowledge of spontaneous reporting with structured educational programs in Korean community pharmacists: a cross-sectional study	1. Pharmacists with private access were less likely to correctly identify SRS content than those who attended structured programs ($p<0.01$). 2. Pharmacists' knowledge was lower regarding reporting of non-prescription products, supplements, and hygiene products than prescription drugs

			($p<0.01$). 3. Structured education programs, alone or in combination, improved SRS knowledge.
4.	Ma et al. (2021)	Immune checkpoint inhibitors -related myocarditis in patients with cancer: an analysis of international spontaneous reporting systems	1. Signal detection indicating Avelumab-related myocarditis was highest with the ROR and PRR methods, while the strongest signal for Ipilimumab was detected with the BCPNN method. 2. This study highlights the potential risk of myocarditis due to ICI use, in line with previous clinical trials, and may serve as a reference for clinical personnel in its use.
5.	Bukic et al. (2019)	Analysis of spontaneous reporting of suspected adverse drug reactions for non-analgesic over-the-counter drugs from 2008 to 2017	1. ADRs were most common in patients ≥70 years (15%), and 5% of reports were from accidental exposure in children. 2. Pharmacists most commonly report ADRs of over-the-counter drugs, and consumer awareness is increasing. 3. Health workers need education on ADR reporting, especially regarding the safety of over-the-counter drugs in the elderly and children.
6.	Kim et al. (2020)	A cross-sectional survey of knowledge, attitude, and willingness to engage in spontaneous reporting of adverse drug reactions by Korean consumers.	1. Positive attitude, SRS awareness, self-efficacy, and ADR counseling experience significantly influenced reporting intention (aOR >1, $p < 0.01$). 2. The importance of enhancing consumer vigilance and empowering self-reporting to strengthen drug safety.
7.	Martin et al. (2022)	Validation of Artificial Intelligence to Support the Automatic Coding of Patient Adverse Drug Reaction Reports, Using Nationwide Pharmacovigilance Data	1. The AI model showed promising performance in automatically coding ADR reports, with consistent results across different approaches. 2. The system has been used by French health authorities since January 2021 to support pharmacovigilance of COVID-19 vaccines. Further validation is needed in other settings.

8.	Létinier et al. (2021)	Artificial Intelligence for Unstructured Healthcare Data: Application to Coding of Patient Reporting of Adverse Drug Reactions	1. The best model for ADR identification was LGBM with AUC 0.93 and F-measure 0.72; external validation showed AUC 0.91 and F-measure 0.58. 2. AI is capable of learning from unstructured data, supporting further studies and development of practical tools for drug safety management.
9.	Destere et al. (2024)	An artificial intelligence algorithm for co-clustering to help in pharmacovigilance before and during the COVID-19 pandemic	1. dLBM identifies drug-ADR specific associations, such as antiplatelet and anticoagulants with bleeding. 2. Together with co-clustering, dLBM is a promising tool for unsupervised detection and exploration of safety signals in large-scale pharmacovigilance databases.
10.	Roosan et al. (2022)	Artificial Intelligent Context-Aware Machine-Learning Tool to Detect Adverse Drug Events from Social Media Platforms	1. The AI algorithm aTarantula was successfully developed to detect warfarin-related ADEs from online forums, with a sensitivity of 84.2% and specificity of 98%. 2. This study demonstrates the potential of aTarantula, which can be further validated on more diverse data.
11.	Gordo et al. (2021)	Root causes of adverse drug events in hospitals and artificial intelligence capabilities for prevention	The analysis shows that AI's capabilities in identification and readout can help prevent ADEs, by addressing misidentification as a major root cause of adverse drug events.

ADR reporting with SRS

Most studies show that ADR reporting through the SRS remains low, influenced by personal, institutional and systemic factors. Asiamah et al., (2022) noted that PV training increased the likelihood of reporting (AOR = 18.78), while legal fear (AOR = 0.15) and time constraints (AOR = 0.3) decreased it. Fang et al., (2017) showed that training, education, and incentives increased compliance with the SRS. Meanwhile, they found that structured education programs contributed to the improvement of reporting knowledge by community pharmacists. Ma et al., (2021) analyzed data from international reporting systems and identified myocarditis signals associated with the use of immune checkpoint inhibitors (ICIs) such as Avelumab and Ipilimumab. Bukic et al., (2019) noted that the age group ≥70 years and children are vulnerable populations to ADRs from over-the-counter drugs. Kim et al., (2020) asserted that positive attitude and counseling experience increase the willingness of ADR reporting by consumers.

ADR Reporting with AI

AI approaches in PV provide promising results in signal detection. Martin et al., (2022) validated an AI model for automatic coding of patient ADR reports nationwide in France, showing high performance in data classification. Létinier et al., (2021) noted that the LGBM model achieved an AUC of 0.93 and F-measure of 0.72 in detecting ADRs from unstructured data. Destere et al., (2024) developed dLBM to identify drug-ADR relationships in large databases, especially during the COVID-19 pandemic. Roosan et al., (2022) developed the aTarantula algorithm that detects ADEs from social media with 84.2% sensitivity and 98% specificity.

Discussion

The findings in this study emphasize the fundamental differences between SRS systems and AI approaches, in terms of methodology, effectiveness, and data coverage. SRS systems, as a traditional approach, have the strength of directly documenting reports from clinical practice, but are limited by reliance on human reporters, risk of bias, delay, and underreporting (Ampadu et al., 2016); Güner & Ekmekci, 2019). These challenges are consistent globally, as revealed by Aagaard et al., (2012) who reported that low-resource countries show very low reporting rates.

Although interventions such as training and incentives improve reporting Fang et al., (2017) and Yu & Lee (2017) the sustainability of interventions and their long-term effects have not been fully measured. Even in countries with developed health systems, patient self-reporting remains low (Worakunphanich et al., 2023). This suggests that the SRS approach is not sufficient to detect the entire spectrum of ADRs, especially in vulnerable populations or in the context of new drug use.

In contrast, AI approaches have significant advantages in terms of speed, efficiency, and data coverage. AI models such as LGBM, dLBM, and aTarantula demonstrate better ADR detection capabilities than traditional methods, especially from unstructured data such as online forums and electronic medical records (Martin et al., 2022; Roosan et al., 2022). This capability is important as a lot of ADR data is hidden in narrative medical records or informal platforms that are not reached by SRS systems.

Furthermore, AI enables predictive analysis and early detection, which is particularly relevant in emergency situations such as the COVID-19 pandemic, where the use of new or off- label drugs is drastically increasing (Destere et al., 2024). This strengthens the argument that the integration of SRS and AI can create a PV system that is more responsive and

adaptive to clinical and global dynamics. However, it should be noted that the use of AI is not without challenges. Issues such as limited external validation, potential algorithm bias, as well as the need for ethical and regulatory oversight, remain a concern (Gordo et al., 2021). The development of a hybrid system between SRS and AI needs to be supported by national policies, digital infrastructure, and increased human resource capacity in the health sector.

4. CONCLUSIONS

Detection of pharmacovigilance signals through SRS still faces challenges of underreporting, reporting delays, and reporter bias. The integration of AI offers an innovative solution with big data analysis capabilities, high accuracy, and detection from unstructured data automatically and in real-time. Evidence from various studies shows that the combination of SRS and AI approaches can complement each other to improve the effectiveness and accuracy of ADR detection. In the future, the development of a hybrid pharmacovigilance system needs to be supported by national policies, health worker training, and a strong digital infrastructure. This strategy is important to realize an adaptive, precise, and proactive drug safety system in the era of digital transformation of healthcare.

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