Artificial Intelligence for Next-Gen Pharmacovigilance and Post-Marketing Surveillance in Evolving the Healthcare Environment

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Abstract
In the rapidly evolving healthcare environment, pharmacovigilance (PV), the science of detecting, assessing, and preventing adverse drug reactions (ADRs) remains an essential part of clinical practice and drug safety governance worldwide. Traditional PV systems rely on voluntary reporting and non-automated data processing, thus leads to low reporting rates, slow signal detection, and poor analytical performance, and fail to keep pace with the growing number of drugs and the volume of data. Post-marketing surveillance (PMS), a cornerstone of PV systems, faces particular strain as the sheer scale of real-world drug exposure data generated after regulatory approval increasingly overwhelms conventional monitoring infrastructure. AI technologies have demonstrated transformative potential across principal PV functions: Natural Language Processing (NLP)-driven pipelines extract ADR signals from electronic health records (EHRs) and scientific literature with enhanced sensitivity, while Machine Learning (ML) classifiers improve signal detection specificity within spontaneous reporting databases such as FDA Adverse Event Reporting System (FAERS) and VigiBase, offering transformative potential for strengthening PMS programs globally. Ethical considerations—including algorithmic bias (prejudice in training data), model opacity, and hallucination risks in generative systems—demand rigorous attention and auditing. With its enormous potential, AI can revolutionise PV from a reactive, resource-heavy field into a proactive, precision-driven safety science reshaping post-marketing surveillance from a passive data collection exercise into a dynamic, real-time risk management system requiring multistakeholder collaboration among industry, regulators, clinicians, and informaticists, supported by validated, transparent, and ethically governed systems.

Keywords: PV; PMS: AI; ML; NLP; ADR; EHRs; Signal detection.

1. Introduction

Pharmacovigilance (PV), the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine-related problems, extending throughout a drug's entire lifecycle, particularly during Phase IV (post-marketing surveillance) and clinical trials. PV is one of the most important foundations of present-day pharmaceutical regulation, involves the ongoing surveillance, assessment, and dissemination of drug safety data throughout the life cycle of a medicine. The historical process of PV emerged directly from the thalidomide tragedy of the late 1950s and early 1960s, which resulted in widespread teratogenic injury and led to the establishment of the WHO Programme for International Drug Monitoring in 1968 (Kothari et al., 2019, p. 60). The regulatory landscape for PV has since changed significantly with the introduction of key regulatory initiatives such as the International Council for Harmonisation (ICH) E2 guidelines, the EU GVP modules, and the FDA's post-marketing safety regulations, which have introduced strong signal detection and risk management requirements for marketing authorisation holders (Mohd. Wasiullah et al., 2025; Prof. M. Wasiullah et al., 2025). However, there are still significant gaps in the traditional system of pharmacovigilance. The underreporting rates in PV, which range from 90% to 95%, are chronic issues that plague spontaneous reporting systems (SRS), which are the backbone of PV worldwide, and are a result of clinician time constraints, uncertainty about causality thresholds, and awareness deficits (Campbell, Gossell-Williams and Mg, 2015, p. 3; Gahr et al., 2017). As of 2024, WHO VigiBase contains over 40 million individual case safety reports (ICSRs), which are large repositories of drug safety signals, but whose effective exploitation requires analytical infrastructure that cannot be manually handled (Brand et al., 2026). Furthermore, the pharmaceutical pipeline is becoming increasingly complex, with the inclusion of biologics, advanced therapy medicinal products (ATMPs), combination products, and novel small molecules, and the ADR landscape is also diversifying, generating multidimensional safety signals that are difficult to identify with the use of conventional disproportionality analysis alone. ADRs are a major problem worldwide. A meta-analysis published in the British Journal of Clinical Pharmacology estimated that approximately 6.5% of hospital admissions in developed countries are due to ADRs, and in the USA, the direct cost of ADRs is estimated to be more than USD 30 billion per year (Everett, 2016, p. 1). The Journal of the American Medical Association (JAMA) estimates that fatal ADRs are the fourth to sixth cause of in-hospital death in the United States, but there is significant variation in estimates based on methodology and population (Giardina et al., 2018, p. 2). This burden is compounded by the lack of PV infrastructure, polypharmacy in ageing

populations, and limited availability of pharmacogenomic testing that might enable identification of high-risk individuals in the future, in low and middle-income countries (LMICs) (Perezcano, 2026). The increasing number of sources of real-world data (RWD), such as EHRs, administrative claims databases, patient registries, mobile health applications, and social media platforms, provide an unprecedented opportunity to complement spontaneous reporting with population-scale safety signals (Lavertu et al., 2021; Hadia et al., 2024). However, deriving structured pharmacovigilance intelligence from these diverse, unstructured, and sometimes noisy datasets requires computational methods that go beyond traditional epidemiological methods (Roux et al., 2005, p. 519; Shamim et al., 2024). AI technologies, including supervised and unsupervised machine learning, deep neural networks, NLP, and the recently emerged large language models (LLMs), can automate, speed up, and enhance nearly every key aspect of contemporary pharmacovigilance, from initial case intake to duplicate detection, benefit-risk assessment, and regulatory reporting (Shamim et al., 2024; Shinde, 2026).

2. METHODOLOGY

A systematic search of electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, was conducted to identify peer-reviewed articles conceptually relevant to the study's objectives. The search strategy targeted literature published primarily between 2000 and 2025. Keywords used were- pharmacovigilance; artificial intelligence; machine learning; natural language processing; adverse drug reactions; signal detection; post-marketing surveillance; large language models; real-world evidence; explainable AI. The eligible studies included original research studies, high impact reviews published in the English language that had evidence of Artificial Intelligence in pharmacovigilance and post marketing surveillance.

3. OVERVIEW OF ARTIFICIAL INTELLIGENCE IN HEALTHCARE AND PHARMACOVIGILANCE

AI is generally defined as the ability of a computational system to execute tasks that typically require human cognitive abilities, such as reasoning, pattern recognition, language understanding, and decision-making (Lin et al., 2023, p. 101832). In healthcare, AI can be found at various levels of methodological complexity, ranging from rule-based expert systems to statistical classifiers, biologically inspired deep learning architectures, and generative foundation models (Sun and Ortíz, 2024, p. 5; Weidener and Fischer, 2024, p. 2). The algorithmic foundation of modern biomedical AI is machine learning (ML) (Athanasopoulou et al., 2022). Supervised ML models, such as logistic regression, random forests, gradient boosting machines (e.g., XGBoost, LightGBM), and support vector machines, learn discriminative mappings from labelled training data and are thus well-suited for classification tasks, such as ADR causality assessment and signal prioritisation (Létinier et al., 2021, p. 393; Imran et al., 2022, p. 583).

Latent structures in unlabelled PV data sets can be identified using unsupervised algorithms, such as k-means clustering, hierarchical agglomerative clustering, and latent Dirichlet allocation, and used to discover novel drug-event associations without prior hypotheses (Zhao, Zou and Chen, 2014, p. 2). Although not as well developed in PV, reinforcement learning could be useful for optimising the sequential decision-making process in a safety signal triage workflow (Chung and Lin, 2024). Multilayered artificial neural networks (ANNs) represent a paradigmatic step beyond shallow ML and are known as deep learning (DL) (Jiang et al., 2022, p. 4). Convolutional neural networks (CNNs) are known to be extremely effective for image pattern recognition and have also been used for 1D sequences via 1D convolution (Ige and Sibiya, 2024; Younesi et al., 2024, p. 8). To capture temporal dependencies in longitudinal clinical data, which are important to identify delayed ADRs and temporal drug interactions, recurrent neural networks (RNNs) and their long short-term memory (LSTM) variants are used (Siebra, Kurpicz-Briki and Wac, 2024, p. 2; Assaf et al., 2025).

Transformer models, which underpin modern LLMs, are the current state of the art for sequence modelling and can understand context-sensitive language across documents of varying length (Wolf et al., 2020, p. 38). In PV, in particular, the majority of pharmacovigilance data is contained within unstructured text, such as case narratives, discharge summaries, social media posts, scientific abstracts, and regulatory submissions, making natural language processing (NLP) central to PV applications (Shamim et al., 2024). In the context of PV, NLP pipelines usually include tokenisation, named entity recognition (NER) to identify drug names and adverse event terms, dependency parsing to extract relationships, and coreference resolution to disambiguate drug names in context ("Proceedings of the 5th Clinical Natural Language Processing Workshop," 2023, p. 102). Inter-source consistency is further improved by named-entity normalisation using biomedical ontologies, such as MedDRA, SNOMED-CT, and the Unified Medical Language System (UMLS) (Bobed et al., 2018, p. 1; Thompson

Table 1. Comparison of artificial intelligence technologies and their pharmacovigilance applications — mechanisms, strengths, and limitations

AI Technology	Core Mechanism	Key PV Applications	Strengths	Limitations	References
Rule-Based Systems	Predefined logical IF-THEN rules	ICSR triage; regulatory compliance checks	Transparent; auditable	Brittle; no learning capability	(Kassekert et al., 2022, p. 439)
Classical ML (RF, XGBoost)	Statistical learning from labelled features	Signal detection; ADR classification; duplicate ID	Interpretable; fast; works with small datasets	Feature engineering required; limited with unstructured data	(Ferreira et al., 2024, p. 2435)
Deep Learning (CNN, LSTM)	Multi-layer neural networks;	EHR mining; image-based diagnostics;	High accuracy; handles raw data	Data-hungry; black-box; computationally	(Létinier et al., 2021, p. 396; Vaz

	automatic feature extraction	temporal ADR patterns		expensive	and Balaji, 2021, p. 1581)
Transformer / BERT Models	Self-attention over token sequences	ADR NER from text; literature mining; case narrative analysis	State-of-art NLP; context-aware	Large training data needed; high GPU cost	(Scaboro et al., 2023; Yokoyama, Natter and Godet, 2023, p. 2)
Large Language Models (GPT-4, Claude)	Generative pre-training at scale; few-shot generalization	Case summarization; PBREP generation; literature triage	Versatile; minimal fine-tuning needed	Hallucination risk; regulatory validation challenge	(Hakim et al., 2024, p. 3; Li et al., 2024)
Graph Neural Networks (GNN)	Message passing on node-edge drug-event graphs	Drug-drug interaction signal detection; pharmacological network analysis	Encodes relational structure	Graph construction complexity; scalability	(Zhong, Barkova and Mottin, 2025, p. 2)
Explainable AI (XAI: SHAP, LIME)	Post-hoc feature attribution or attention visualization	Regulatory justification; bias auditing; causal plausibility checks	Increases trust; regulatory-friendly	Approximations; may not reflect true model logic	(Ward et al., 2021, p. 106415; Suryadevara, Priya and Sharma, 2026)
Federated Learning	Distributed gradient aggregation without data sharing	Multi-institutional EHR-based PV model training	Privacy-preserving; scalable	Communication overhead; heterogeneity challenges	(Hai et al., 2022, p. 3; Meduri et al., 2024)

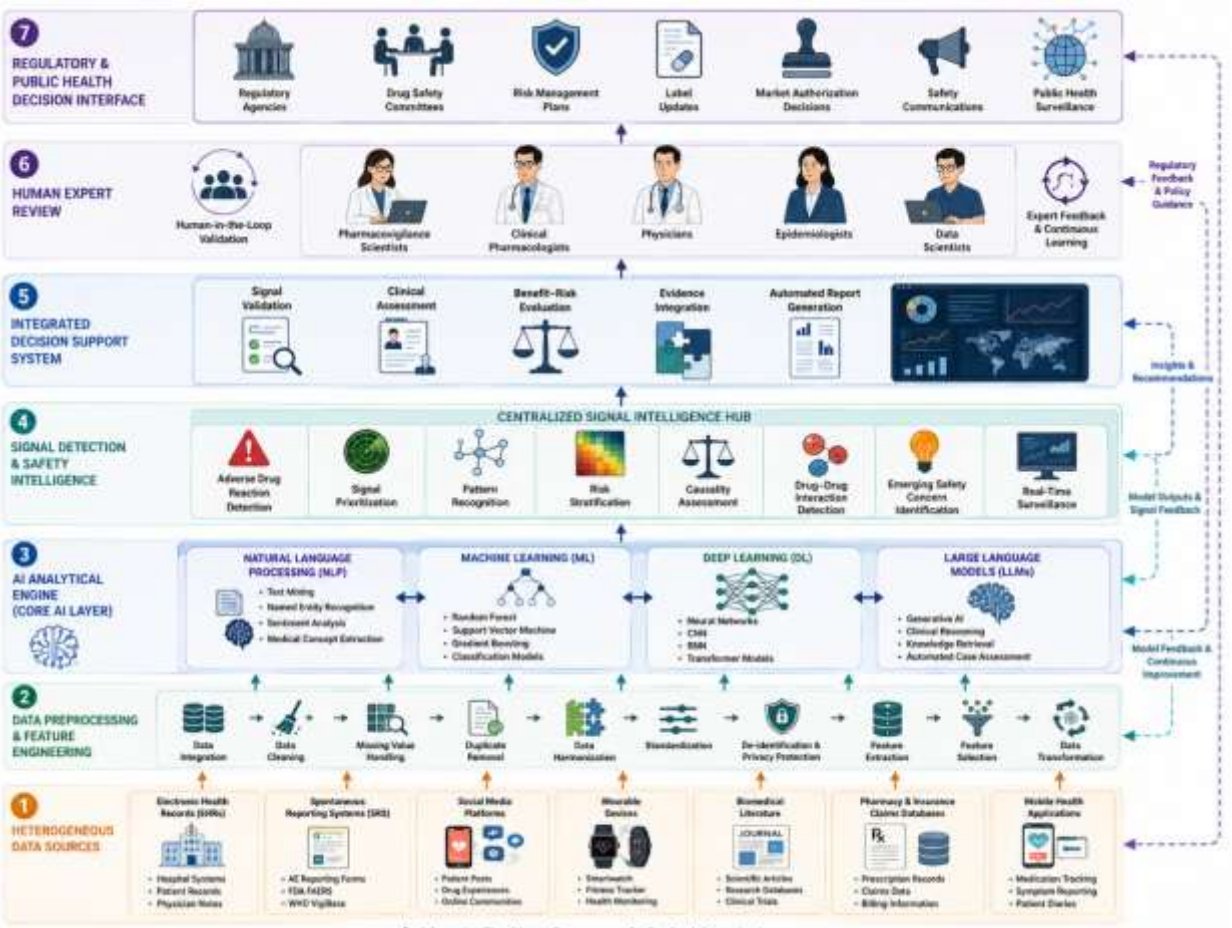

Fig 1. Hierarchical architecture of AI-driven pharmacovigilance systems.

The framework illustrates the progression from heterogeneous real-world healthcare data sources to advanced artificial intelligence analytical modules, including natural language processing, machine learning, deep learning, and large language models, for enhanced post-marketing drug safety surveillance. et al., 2018, p. 2). Explainable AI (XAI) has become a conceptually and regulatory-driven area of interest (Suryadevara, Priya and Sharma, 2026). Post-hoc or inherent interpretability can be achieved using techniques such as SHAP (SHapley Additive exPlanations), LIME (Local

Interpretable Model-agnostic Explanations), gradient-weighted class activation mapping (Grad-CAM), and attention visualisation (Bharati, Mondal and Podder, 2023, p. 1434). In the context of pharmacovigilance, XAI plays a crucial role in ensuring regulatory acceptance, verifying clinical plausibility, and providing medico-legal accountability, allowing AI-generated safety signals to be explained and scrutinised by human experts (Ferreira-da-Silva, Cruz-Correia and Ribeiro-Vaz, 2025; Suryadevara, Priya and Sharma, 2026).

4. AI APPLICATIONS IN PHARMACOVIGILANCE

The use of AI technologies in the pharmacovigilance workflow is multi-faceted, from case processing to signal science, risk communication to dedicated therapeutic area surveillance. The major application areas are discussed in detail below, along with the mechanisms and a critical appraisal of the existing evidence.

4.1 Automated Case Processing

One of the most advanced and market-ready PV AI applications is automated case processing (Kassekert et al., 2022, p. 439). Traditionally, ICSR processing involves trained pharmacovigilance professionals who spend an estimated 35-45 minutes per ICSR on the labour-intensive task of extracting, categorising, and coding adverse events from various types of source documents (Ledieu et al., 2018, p. 8). Oracle Argus AI-augmented modules and the Veeva Vault Safety platform have been shown to save 60-80% of this time by using AI-driven systems that utilise NLP pipelines, rule-based logic, and ML classifiers. The Octavia system built by Trifacta and tested in Phase IV scenarios achieved F1-scores of >0.87 in the entity extraction task for unstructured case narratives. Multi-label classification models trained on MedDRA hierarchies allow for concurrent identification of primary and secondary ADR terms with significantly higher consistency than manual coding (Martin et al., 2022, p. 535) and offer a way to mitigate the inter-rater variability, which remains a quality issue in case processing centres around the world (Schroll, Maund and Gøtzsche, 2012, p. 1; Fusaroli et al., 2025, p. 2).

4.2 Signal Detection and Prioritization

The scientific core of pharmacovigilance is signal detection, or the identification of new or partially described drug-event relationships from the large volumes of data that are accumulated in safety databases. The traditional disproportionality methods, such as the Reporting Odds Ratio (ROR), Proportional Reporting Ratio (PRR) and the Bayesian Confidence Propagation Neural Network (BCPNN) that powers the signal detection engine of VigiBase, continue to be important, but are vulnerable to masking effects, competitive inhibition of signals and confounding by indication (Khouri et al., 2021, p. 2). ML-based extensions of these methods overcome several of these limitations: regularised logistic regression models account for co-prescription patterns of drugs; Bayesian hierarchical mixture models account for temporal trends in reporting rates; and graph neural networks (GNNs) leverage the network of drug-drug interactions to put emergent signals in their context. The use of ensemble ML methods with FAERS data increased the PPV of the detected signals by 23% compared with PRR alone and resulted in significantly lower FDRs. Multivariate scoring models that take signal strength, disproportionality, temporal clustering analysis, and literature evidence of mechanism into account further increase the efficiency of human expert review (Yamamoto et al., 2023, p. 377).

4.3 Adverse Drug Reaction Prediction

One of the frontiers of application is predicting ADRs before clinical manifestation, which has a huge impact on personalised medicine. Pharmacogenomic ML models that combine information on genetic variants, drug-metabolizing pathways, and patient-specific comorbidity profiles have demonstrated the ability to predict idiosyncratic ADRs with clinically relevant accuracy. A benchmark study published in Nature Communications (2023) used graph convolutional networks to predict previously unknown hepatotoxicity risks for a number of approved drugs when applied to a drug-target interaction network (Zhao et al., 2024, p. 4; Xiao et al., 2025). AUROC scores for drug-induced liver injury (DILI) prediction have exceeded 0.85 with hybrid deep learning models, integrating molecular fingerprints, protein structure features, and electronic health record (EHR) covariates, an achievement historically challenging for traditional cheminformatics methods (Zhao et al., 2024, p. 4). Sequence-to-sequence models trained on temporal EHR data can help identify at-risk patient subpopulations in the prescribing decision process, paving the way for AI-driven ADR prediction to become an integral part of precision prescribing support systems.

Table 2. Machine learning algorithms and their mechanisms in adverse drug reaction detection

Algorithm	Type	Mechanism in PV Context	ADR Detection Performance (approx.)	Key Studies
Logistic Regression	Supervised ML	Baseline classifier for ADR signal filtering; regularized for high-dimensional feature spaces	AUROC 0.70–0.80	(Létinier et al., 2021, p. 398)
Random Forest	Ensemble / Supervised ML	Aggregates decision trees to classify drug-event pairs; importance scores guide signal triage	AUROC 0.80–0.88	(Bae et al., 2021, p. 1)
XGBoost / LightGBM	Gradient Boosting	Sequential error-correcting trees; handles class imbalance via	AUROC 0.85–0.91	(Crisafulli et al., 2024, p. 7)

		scale_pos_weight; fast inference		
LSTM / BiLSTM	Recurrent Deep Learning	Captures sequential temporal dependencies in longitudinal EHR ADR event sequences	F1 0.82–0.89 (event extraction)	(Murphy et al., 2023, p. 16)
BERT / BioBERT	Transformer NLP	Token-level ADR entity recognition and causality classification from clinical text	F1 0.88–0.94 (NER tasks)	(Yang et al., 2020, p. 1939)
Convolutional Neural Network	Deep Learning	Local feature detection in sequence or image data; 1D CNN for text classification	F1 0.83–0.88	(Suárez-Paniagua and Segura-Bedmar, 2018, p. 2)
Graph Convolutional Network	Graph Deep Learning	Drug-protein-event network analysis; novel ADR prediction via guilt-by-association	AUROC 0.87 (DILI prediction)	(Zhao et al., 2024, p. 4)
Bayesian Neural Network (BCPNN)	Probabilistic DL	Posterior probability estimation of drug-event association; uncertainty quantification	IC_{025} threshold-validated	(Gamaleldin, Abdelhalim and Abraham, 2024, p. 6)

4.4 Duplicate Detection

One issue that is often overlooked but has a large impact on operations in PV is duplicate detection, meaning that the same adverse event could be reported in multiple sources, increasing the chances of it being captured in the signal, and skewing the safety databases. In the absence of accurate or pseudonymized patient identifiers, traditional string-matching and rule-based methods have high false negative rates. The sensitivity of duplicate identification can be significantly increased by using ML-based probabilistic record linkage, which leverages features such as demographic congruence, event-onset date similarity, reporter type, and concomitant medication overlap (Barrett et al., 2026).

4.5 Literature Screening Automation

The scientific literature is one of the required sources of data in ICH E2D guidelines, and marketing authorisation holders are required to monitor and review the safety information that emerges on a continuous basis (Pontes, Clément and Rollason, 2014, p. 475). One of the most resource-intensive PV activities is the traditional manual screening of databases such as PubMed, Embase, and regional databases for publications relevant for ADR. AI-enhanced literature screening uses multi-stage NLP classifiers, with a first-pass binary relevance filter that identifies drug names with>98% recall and reduces manual effort by 65-75%, followed by fine-grained extractors for ADR terms, study populations, and causality assessment. Operationalisation of these pipelines in a regulatory-grade environment is now available using tools such as Aurea Intelligence's Iris and Elsevier's PharmaPendium, and it meets the EMA and FDA literature review expectations (Martenot et al., 2022, p. 2).

4.6 NLP for Adverse Event Extraction from Clinical Text

The adverse event extraction from unstructured clinical text using NLP has been well validated in the EHR setting. The i2b2 NLP challenge datasets and the n2c2 shared tasks have been used to evaluate NLP system performance on medication and ADR extraction, and the best performance has been consistently achieved by the latest transformer networks (BioBERT, ClinicalBERT, PubMedBERT) as compared with previous recurrent networks. Specialized transformer networks, such as PubMedBERT, have achieved high F1-scores for adverse drug event extraction on benchmark datasets, with top systems demonstrating F1-scores around 0.90 or higher (Yang et al., 2020, p. 1939; Martenot et al., 2022, p. 12). In recent large-scale applications, the system has been shown to identify previously unreported ADRs in real-world clinical corpora, thereby directly addressing the spontaneous reporting gap.

4.7 AI in Social Media Pharmacovigilance

Social media is a great and largely untapped source of pharmacovigilance data. Every day, millions of stories about patients' experiences with medications are posted on platforms such as Twitter/X, Reddit's r/medicine, MedHelp, and patient forums, often detailing adverse events weeks or months before they are reported as ICSRs. The particular challenges of NLP systems applied to social media PV include non-standard terminology, abbreviations, sarcasm, and polysemous expressions, which necessitate the use of colloquial, context-aware lexicons and classification methods (Pappa and Stergioulas, 2019, p. 124). Social listening platforms have been optimised using custom bioNLP models trained on health-related social corpora and perform competitively on health-specific ADR identification benchmarks (Guellil et al., 2026).

4.8 AI-Assisted Benefit-Risk Assessment

Benefit-risk assessment (BRA) is one of the most important (Musuamba et al., 2023, p. 41) and challenging (Cracowski et al., 2024) tasks in regulatory pharmacology. BRA can benefit from AI in several ways: AI can be used to structure data extracted from clinical trial databases (Teodoro et al., 2025); to simulate risk-benefit trade-offs using a probabilistic model (Kleinstreuer and Härtung, 2024, p. 744); and to generate natural-language benefit-risk profiles from various source documents (Huang et al., 2023, p. 3). The Multi-Criteria Decision Analysis (MCDA) framework, endorsed by the EMA (Chisholm, Sharry and Phillips, 2022), can be augmented with computational means, such as ML-based weighting

optimization (Sarkar, Goswami and Gupta, 2026). In the real world, where randomized controlled trials are often not conducted and confounding by indication, channeling bias, and adherence heterogeneity are likely to affect the results of traditional analyses, causal inference models, such as propensity score-based methods and targeted maximum likelihood estimation (TMLE), can be applied to RWD to estimate real-world benefit-risk ratios that complement the data from RCTs (Gruber et al., 2023; Anagnostopoulos et al., 2025).

4.9 AI in Vaccine Pharmacovigilance

The most specific issues in vaccine pharmacovigilance concern signal detection, especially during mass vaccination campaigns, where the likelihood of temporal coincidence (rather than causal association) is high. The use of AI-based self-controlled case series (SCCS) extensions and sequential probability ratio tests (SPRT) in near real-time provides a much more efficient analytical approach than traditional epidemiology to differentiate vaccine-attributable events from background rates (Li et al., 2021, p. 1). In the context of the COVID-19 vaccine rollout, ML algorithms using systems like VAERS have been applied to identify vaccine-related adverse events with enhanced signal detection (Dong et al., 2023, p. 173). Graph-based network analyses of co-reported symptoms provided additional insight into novel vaccine adverse-event phenotypes beyond single-event analysis (Beatty et al., 2021, p. 9; Buoninfante et al., 2022, p. 1; Burn et al., 2022, p. 4).

Table 3. Representative AI tools and platforms currently deployed in pharmacovigilance operations

Platform / Tool	Developer	PV Function	AI Technology	Regulatory Adoption	References
Oracle Argus AI	Oracle Health Sciences	ICSR processing; duplicate detection; case triage	NLP; ML classifiers	FDA-compliant; widely used by MAHs	(Shamim et al., 2024)
Veeva Vault Safety	Veeva Systems	End-to-end ICSR management; narrative generation	NLP; workflow AI	EMA/FDA-aligned; GxP-validated	(Mintaş and Sevimli-Gür, 2024, p. 6)
Empirica Signal	Oracle Health Sciences	Signal detection from FAERS/EudraVigilance	Bayesian methods; ML extensions	Used by multiple regulatory agencies	(Crisafulli et al., 2024, p. 7)
VigiLyze / VigiBase	Uppsala Monitoring Centre (WHO)	Global signal detection; ICSR analytics	BCPNN; ML-augmented disproportionality	WHO/ICH standard	(Badria and Elgazar, 2024, p. 5)
Aurea Intelligences Iris	Aurea Intelligences	Literature monitoring; relevance classification	BERT-based NLP; supervised classifiers	EMA-compliant literature monitoring	(Yang and Kar, 2023)
ArisGlobal LifeSphere	ArisGlobal	Case processing; signal detection; regulatory reporting	NLP; ML; RPA	ICH E2B(R3); FDA/EMA submission-ready	(Nwankwo et al., 2024, p. 814)
Saama Technologies LSAC	Saama	Clinical safety analytics; aggregate reporting support	ML; NLP; visual analytics	Validated in pharma industry settings	(Mishra and Gupta, 2024)
Sentimoto / Treato	Digital health companies	Social media ADR signal mining	Social NLP; sentiment analysis	Research/supplementary PV tool	(Ferreira et al., 2024, p. 2443)

Fig 2. Workflow of an AI-based pharmacovigilance signal detection system.

Adverse event information from FAERS, EudraVigilance, and electronic health records is ingested and processed through NLP-driven extraction and MedDRA normalization. Machine learning algorithms, disproportionality analyses, and Bayesian inference identify potential safety signals, which are further contextualized using graph neural network–based pharmacological knowledge graphs. Prioritized signals are presented through an intelligent ranking dashboard for expert pharmacovigilance review, ultimately informing regulatory decision-making and public health interventions within a continuously learning drug safety ecosystem.

4.10 AI in Oncology Pharmacovigilance

The high background rate of severe adverse events, intrinsic to the disease and to cytotoxic or immunomodulatory treatment regimens, poses a challenge for oncology pharmaco-vigilance, as attribution is particularly difficult (Baldo et al., 2018, p. 832). Structured EHR data from an oncology-specific registry (e.g., SEER-linked data) can be used to train deep learning models to detect patterns of chemotherapy-induced toxicity, which include cardiotoxicity, immune-related adverse events (irAEs), and hematological toxicity, with sensitivities that are superior to the traditional Common Terminology Criteria for Adverse Events (CTCAE) grading by clinicians in retrospective audits (Bakouny et al., 2025; Wilson et al., 2026). In post-marketing safety surveillance, there is an urgent need to effectively monitor irAEs across the growing number of immuno-oncology drugs (Kim et al., 2024, p. 2). Natural language classifiers trained on oncology clinical notes have shown near-expert performance in identifying and grading irAEs across a wide range of immunotherapy regimens. Furthermore, utilizing machine learning to analyze diverse patient cohorts allows for the identification of subgroups prone to specific toxicities, thereby facilitating specialized monitoring and personalized risk management (Zou, Natsiavas and Gottlieb, 2024).

5. ARTIFICIAL INTELLIGENCE IN POST-MARKETING SURVEILLANCE

Post-marketing surveillance (PMS) is an extension of the safety evaluation of medicinal products from the more homogeneous clinical trial population to the more heterogeneous routine clinical practice population. This methodological shift from pre-approval to post-approval safety science requires a fundamental shift: from hypothesis-confirming randomised trials to hypothesis-generating, signal-detecting, and risk-characterising analyses of administrative, clinical, and real-world data sources (Fusaroli et al., 2024, p. 593).

The main infrastructure for generating safety signals in the post-marketing period is still spontaneous reporting systems, such as the FDA's FAERS (2+ million reports annually), the EMA's EudraVigilance, the WHO's VigiBase, and national systems, such as the UK Yellow Card scheme and the Netherlands' Lareb database. AI has made strides in these systems in several ways. Automated case narratization from structured fields helps to minimise manual effort and enhance completeness metrics. Triage models using ML can categorise incoming reports by clinical urgency and novelty, and funnel limited pharmacovigilance resources toward the highest-priority signals (Shwetali, 2025). Dynamic signal landscapes are created with real-time dashboards that use disproportionality algorithms with additional classifiers using Bayesian networks for pharmacovigilance scientist review. Perhaps the most information-rich source of real-world data for PMS is EHRs. A distributed network, such as the FDA Sentinel System (which has >400 million patient-years of data), PCORnet, and the European Health Data Space, has enabled large-scale EHR mining studies to show the power of AI to detect safety signals at population scale with statistical power that is unattainable in spontaneous reporting analyses (Shamim et al., 2024).

Federated query architectures enable multi-institutional analyses without centralising sensitive patient data, a constraint in PV using EHRs (Meeker et al., 2015). Within a health system, deep phenotyping algorithms can be developed using longitudinal EHR data to identify ADR phenotypes defined by laboratory abnormalities, prescription changes, diagnostic codes, and/or free text, thereby achieving greater sensitivity than diagnosis-code-only surveillance (Nwokedi et al., 2025). Wearable devices and digital biomarkers are at the cutting edge of collecting real-world data for pharmacovigilance (Alsaedi et al., 2024).

Drug-induced perturbations in physiology can be detected in near real time from continuous streams of physiological data collected from smartwatches, implantable cardiac monitors, and remote patient monitoring platforms, including heart rate variability, ECG morphology, activity, and sleep architecture (Alsaedi et al., 2024). The feasibility of detecting drug-induced QT prolongation signals from consumer-grade PPOx data on Apple Watch has been demonstrated by various studies (Strik et al., 2020). The use of signals from wearables, combined with AI-based algorithms for anomaly detection, represents a new, rapidly evolving paradigm for proactively monitoring ADR in ambulatory populations, especially for drugs with potential cardiovascular, neurological, or metabolic side effects (Alsaedi et al., 2024).

The implementation of pharmacogenomics in AI-enhanced PMS can facilitate the identification of subgroups and risk stratification that cannot be done at the population level with standard surveillance (Lauschke and Ingelman-Sundberg, 2026). Combining pharmaco-genomic and EHR data has led to the development of ML models that have been able to predict signatures of genes and drugs that are associated with severe cutaneous adverse reactions (SCARs), anticoagulant-related bleeding complications, and statin-induced myopathy with a high degree of accuracy that is enough to help develop clinical decision support systems (Kidwai-Khan et al., 2022, p. 1).

The growing number of direct-to-consumer genomic datasets and biobank cohorts with EHR data (such as UK Biobank and the All of Us Research Program) further underscores the potential of AI-driven-pharmacogenomic surveillance at scale (Denny et al., 2017, p. 418).

Table 4. Comparative overview of traditional versus AI-augmented post-marketing surveillance across key operational and scientific dimensions

Dimension	Traditional PMS	AI-Augmented PMS	References
Primary data source	Spontaneous adverse event reports	Multi-source: SRS + EHR + social media + wearables + genomics	(Haga, 2024)
Signal detection latency	Weeks to months (batch analyses)	Near real-time continuous monitoring	(Zack et al., 2025)
Case processing speed	30–45 minutes per complex ICSR	60–80% time reduction; automated triage in seconds	(Nwankwo et al., 2024, p. 810)
Literature monitoring	Manual PubMed/Embase review	NLP-automated; 98% recall with 65–75% workload reduction	(Taherdoost and Ghofrani, 2024)
Duplicate detection	Rule-based string matching; ~70% sensitivity	ML probabilistic linkage; F1 0.90–0.95	(Patel et al., 2025)
ADR prediction capability	Reactive; signal detected post-occurrence	Predictive; prospective risk stratification per patient	(Crisafulli et al., 2024, p. 7)
Bias management	Implicit; not systematically addressed	Systematic algorithmic bias auditing possible	(Jakka et al., 2025)
Regulatory reporting speed	Days to weeks for aggregate reports	AI-assisted drafting reduces turnaround by 40–60%	(Abdelhalim et al., 2022, p. 6)
Data volume capacity	Limited by human analyst bandwidth	Scalable to millions of records with cloud AI infrastructure	(Niazi, 2023, p. 2698)
Pharmacogenomic integration	Rarely incorporated routinely	Embedded in precision PV ML models	(Huang et al., 2025, p. 19)

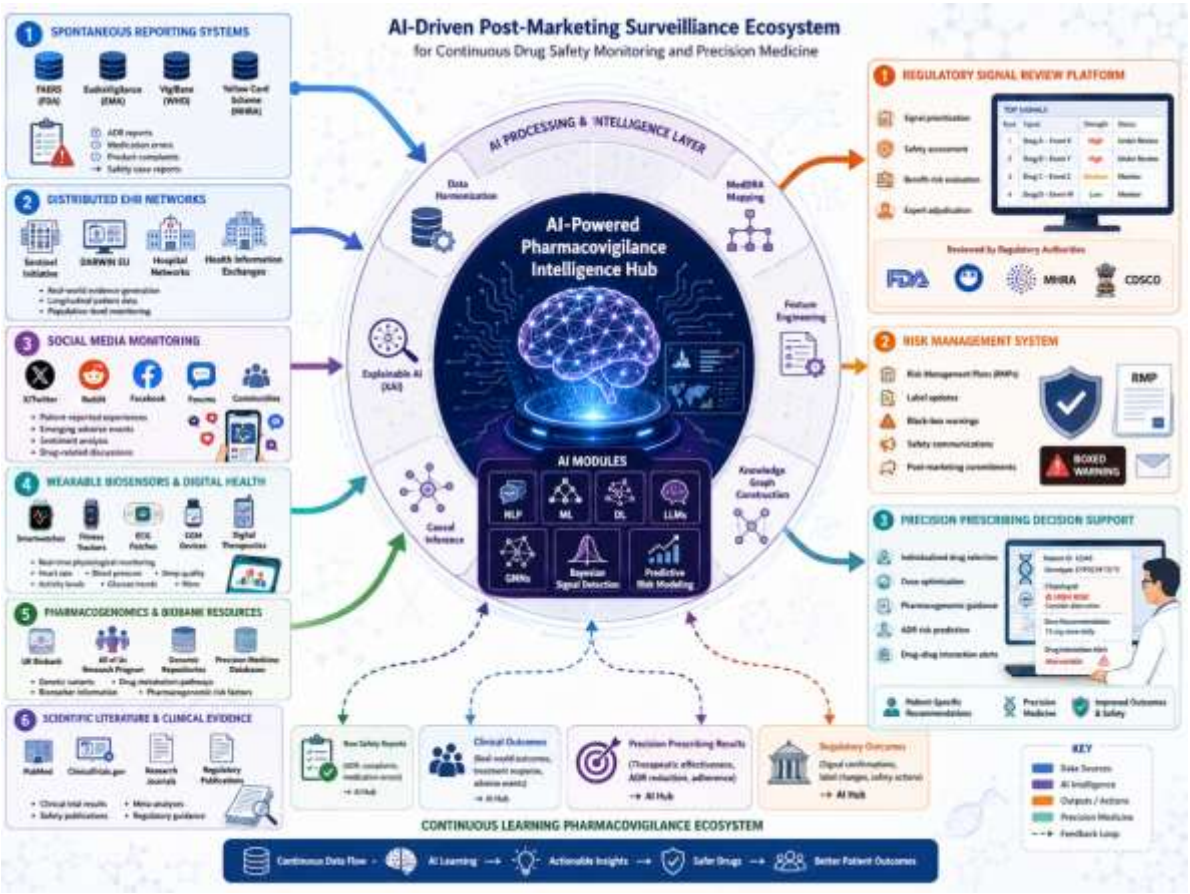

Fig 3. AI-driven post-marketing surveillance ecosystem.

Multiple real-world and biomedical data streams—including spontaneous reporting systems, distributed electronic health record networks, social media monitoring, wearable biosensors, pharmacogenomic biobanks, and scientific literature—converge within a centralized AI analytics hub. Advanced computational methods including NLP, machine learning, deep learning, graph neural networks, and predictive modeling transform heterogeneous data into actionable safety intelligence. Outputs support regulatory signal review, dynamic risk management strategies, and precision prescribing decision-support systems, establishing a continuously learning pharmacovigilance ecosystem for proactive drug safety monitoring and personalized healthcare.

6. ROLE OF LARGE LANGUAGE MODELS AND GEN-AI IN PHARMACOVIGILANCE

Large language models (LLMs) are a qualitative improvement over domain specific NLP models and are capable of natural language understanding and generation in ways never before achieved: they are pre-trained on vast amounts of text from a wide variety of sources. LLMs, such as GPT-4, Claude, Automated summarisation of narratives and the generation of case reports is an LLM application in PV with potential to enhance efficiency (Roemming et al., 2025) asks with little or no task-specific fine-tuning, a phenomenon known as few-shot generalisation. The first LLM (Hakim et al., 2024, p. 4), significantly alleviating medical writing workloads (Roemming et al., 2025), summarisation of narratives and the generation of case reports. LLMs can automate the creation of structured ICSR summaries that adhere to ICH E2B(R3) formatting guidelines, significantly alleviating medical writing workloads. On the other hand, they can take short, structured data fields and flesh (Li et al., 2024); LLMs also demonstrate superior zero-shot generalisation (Jahan et al., 2024) to out-of-sample PV-relevant drug names and adverse event types (MedDRA) compared to previous supervised classifiers. However, LLMs also have a known and significant failure mode: generating seemingly confident but factually incorrect information, commonly known as hallucination. For pharmaco-vigilance, where critical decisions are made based on the correctness of the information on adverse events, the medico-legal and patient safety implications are great when case details are hallucinated, literature references are fabricated, or MedDRA terms are assigned incorrectly. Studies have shown that when LLMs are used to create pharmacovigilance case narratives, the outputs can be clinically plausible but factually inconsistent (Hakim et al., 2024, p. 1). To mitigate these risks, retrieval-augmented generation (RAG) methods can be used to ensure that the outputs of LLMs are based on verified document repositories, constrained decoding using validated ontologies can be used to ensure consistency across the outputs, and hybrid approaches that require human review of PV content generated by AI can be used. Generative AI also opens up new possibilities in PV education, PV signal communication, and PV regulatory writing. The ability to automatically generate sections of Risk Management Plans (RMPs) (Praveen, 2023), Dear Healthcare Professional (DHCP) letters, and Periodic Benefit-Risk Evaluation Reports (PBRERs) from structured safety databases is an emerging capability that has been demonstrated to offer efficiency benefits. The reliability and regulatory fitness of these applications are likely to be significantly enhanced over the next 2-3 years through the pharmacovigilance-specific adaptation of LLMs, including fine-tuning on annotated PV corpora, reinforcement learning from human feedback (RLHF) by PV experts, and tool augmentation that enables structured database queries (Matheny et al., 2024).

Table 5. Potential applications, patient safety benefits, key risks, and mitigation strategies for generative AI and large language models in pharmacovigilance

Application	Potential Benefit	Key Risk	Mitigation Strategy	References
Automated ICSR narrative generation	Reduces medical writing burden; ICH E2B(R3) compliance	Hallucinated event details; incorrect chronology	Human expert review; RAG grounding	(Shamim et al., 2024)
Benefit-Risk Report (PBRER) drafting	Accelerates aggregate report generation	Fabricated literature citations; misattributed statistics	Citation verification pipelines; hybrid human-AI authorship	(Botsis, Ball and Norén, 2023, p. 2)
Literature relevance triaging	Rapid zero-shot classification of new drug/ADR literature	Misclassification of safety-critical publications	Human verification of rejected literature flagged by confidence thresholds	(Kadi et al., 2025, p. 2)
Medical summarization from EHR	Clinician decision support; ADR recognition prompts	Sensitive data exposure; GDPR/HIPAA compliance risk	On-premise deployment; differential privacy; audit logging	(Matheny et al., 2024)
Case narrative translation (multilingual)	Enables global signal integration across languages	Idiomatic medical term mistranslation affecting MedDRA coding	Medical translator validation; MedDRA ontology-constrained output	(Hakim et al., 2024, p. 3)
Regulatory query response drafting	Rapid first-draft regulatory correspondence	Incorrect regulatory claim; legal liability	Legal review gate; not for final submission without expert edit	(Gao et al., 2025)
Patient-facing ADR communication	Personalized medication risk communication	Oversimplification; inappropriate reassurance	Clinician oversight; communication scientist review	(Ong et al., 2025)

7. REGULATORY AND ETHICAL CONSIDERATIONS

The regulatory world has increasingly acknowledged the potential of AI in pharmacovigilance and has also started to define a framework for the governance of AI in this field. The FDA's action plan on AI/ML-based software as a medical device (SaMD) for 2021 and (Awad et al., 2023, p. 3)its draft guidance on the use of artificial intelligence in drug development in

2023 indicate the agency's plans to implement flexible, risk-proportionate regulatory frameworks that can keep up with the fast-changing AI landscape. In particular, the FDA's notion of predetermined change control plans (PCCPs) enables AI systems to change within a predetermined scope without needing (Hines et al., 2019, p. 403) the reflections on the use of AI in regulatory decision-making (Pinheiro et al., 2024) as new PV data come in, models (Pinheiro et al., 2024) and the work of the European Health Data Space (EHDS) (Hunsel and Kant, 2025, p. 7) agency has expressed its stance in the EMA Regulatory Science Strategy to 2025 and the reflections on the use of AI in regulatory decision-making.

Table 6. Ethical challenges in AI-driven pharmacovigilance: specific manifestations and evidence-based mitigation strategies

Ethical Challenge	Specific PV Manifestation	Recommended Mitigation	References
Algorithmic bias	Weber effect; notoriety bias; underreporting in minorities skews model training	Stratified model validation; adversarial debiasing; representative training data curation	(Shamim et al., 2024)
Lack of transparency (black-box AI)	DL model signals unexplainable to regulators; causality assessment opaque	Mandatory XAI integration (SHAP, LIME, attention maps); model cards publication	(Othman et al., 2025)
Hallucination in generative AI	Fabricated ADR details in AI-generated narratives; incorrect MedDRA coding	RAG pipelines; constrained decoding; mandatory human review gates	(Gao et al., 2025)
Data privacy violations	EHR mining without sufficient de-identification; GDPR/HIPAA breach risk	Differential privacy; federated learning; DPA impact assessments before deployment	(Suryadevara, Priya and Sharma, 2026)
Medico-legal accountability gap	Unclear liability when AI misses a signal resulting in patient harm	Clear responsibility allocation in MAH SOP; AI as decision-support, not decision-maker	(Ahire et al., 2024, p. 29)
Reproducibility deficit	AI PV studies not replicable; models not publicly released	Mandatory TRIPOD-AI reporting; open-source code; pre-registered validation studies	(Chavhan and Uplenchwar, 2024)
Digital divide / inequity	AI benefits concentrated in high-income countries with data infrastructure	WHO-led capacity building; open AI PV tools for LMIC regulatory agencies; federated networks	(Kassekert et al., 2022, p. 446)
Informed consent for AI analytics	Patients unaware their EHR data used for AI PV model training	Transparent data governance; opt-out mechanisms; GDPR Article 22 compliance	(Ferreira et al., 2024, p. 2443)

The Big Data Taskforce of EMA and the work of the European Health Data Space (EHDS) give the necessary structure to AI-based analytics (Burns et al., 2023, p. 5). A's DARWIN EU network is a visionary initiative that is a federated data analytics infrastructure for EU-wide real-world evidence generation for regulatory decision-making, with an increasing number of AI-based analytical modules. The EU AI Act (which came into effect in August 2024) considers AI systems used in pharmacovigilance to be high-risk applications, which require conformity assessment, transparency requirements, human oversight, and post-deployment monitoring. Probabilistic AI-based signal detection is now part of the analytical services provided by the World Health Organization (WHO) through its Collaborating Centre at the Uppsala Monitoring Centre (UMC), including VigiLaze and VigiBase (Ghuge, 2025). WHO's 2023 recommendations on the use of AI in health highlight the need for equitable access, bias reduction, and adaptability to local contexts, as patterns of drug use and comorbidity may vary significantly between LMIC and HIC settings, and reporting practices differ across settings. Pre-deployment validation studies, clear reporting of performance metrics across demographic sub-groups, and clear human accountability (Chhikara and Hammad, 2025, p. 1) for AI-driven safety decisions are required by the CIOMS Working Group XI report on pharmacovigilance principles and the CIOMS AI guidance framework.

One of the most significant ethical issues of PV with AI is algorithmic bias (Chhikara and Hammad, 2025, p. 1). Spontaneous reporting systems also suffer from reporting biases such as the Weber effect (more reports in the first two years after launch), notoriety bias after safety communications, and systematic underreporting in elderly, paediatric, and minority ethnic populations, which are also propagated into the data used to train ML models and can result in models that detect signals differently in overrepresented populations (Cutroneo et al., 2024, p. 7). To achieve fair signal detection across a diverse patient population, prospective bias auditing, stratified performance evaluation, and adversarial debiasing techniques are required (Zhao et al., 2022, p. 470). Data privacy is a top priority: AI systems working with EHR and genomic data need to adhere to the EU General Data Protection Regulation (GDPR), the US HIPAA, and similar national regulations (Gamaleldin, Abdelhalim and Abraham, 2024, p. 16), and to incorporate differential privacy, secure multi-party computation, and comprehensive data governance measures. The medico-legal responsibility for PV decisions made by AI

remains unresolved and is conceptually challenging (Gao et al., 2025). In most jurisdictions, responsibility is unclear among the system developer, marketing authorisation holder, and regulatory authority when an AI system fails to recognise a safety signal that is later linked to patient harm (Zhang and Zhang, 2023, p. 9). Meaningful human control has become an increasingly common term in regulatory guidance, but it is not yet consistently implemented in practice in industry, especially in high-stakes safety scenarios, where the recommendation is not subject to substantive human review but rather to a pro forma sign-off (Suryadevara, Priya and Sharma, 2026).

8. CHALLENGES AND LIMITATIONS

While significant strides have been made, the adoption of AI in pharmacovigilance also faces numerous technical, organizational, and regulatory challenges that must be overcome to fully leverage the potential of these technologies in this field. Fundamental issues continue to be data indicates that case narratives are often less informative than they could be; a review found an average of only 12.7 out of 26 potentially important data elements were included in initial reportsdels, which is often not the case in PV real-world applications. The quality of EHR data is extremely uneven between institutions, and the missingness is often non-random, leading to systematic biases in models derived from the data and learned by ML (Honeyford et al., 2022, p. 4).

A prerequisite for cross-institutional model generalisability is the harmonisation of terminology used in ADR across MedDRA versions, regional coding conventions, and -

Table 7. Barriers to large-scale implementation of artificial intelligence in pharmacovigilance operations

Barrier Category	Specific Challenge	Impact Severity	Potential Solution	References
Data quality	Incomplete ICSRs (30–60% completeness); missing narrative fields	High	AI-assisted completeness prompting at data entry; NLP imputation frameworks	(Ward et al., 2026, p. 1)
Interoperability	Heterogeneous EHR systems; non-standardized coding across jurisdictions	High	HL7 FHIR adoption; MedDRA/SNOMED harmonization; OMOP CDM for EHR networks	(Ge, Chan and Yang, 2024, p. 2663)
Model drift	PV data distribution shifts as prescribing and reporting patterns evolve	High	Continuous model monitoring; automated drift detection; scheduled retraining pipelines	(Wacholder et al., 2026, p. 1248)
Black-box interpretability	DL models produce unexplainable outputs unacceptable to regulators	High	Mandatory XAI layers; preference for inherently interpretable models where feasible	(Fierro-Monti, 2026, p. 28)
Validation gaps	Absence of standardized AI PV benchmarks; low reproducibility rates	High	TRIPOD-AI adoption; public benchmark datasets; regulatory sandbox testing	(Chothani et al., 2026, p. 10)
Bias in training data	Weber effect; demographic underrepresentation in reporting systems	Moderate–High	Bias audits; stratified sampling; adversarial fairness constraints	(Posner, Yannuzzi and Prensner, 2023, p. 13)
Infrastructure costs	GPU compute; MLOps platforms; data science talent inaccessible to SMEs	Moderate	Cloud AI-as-a-service PV platforms; CRO AI partnerships; open-source toolkits	(Takahashi, Tateishi-Karimata and Sugimoto, 2025, p. 23)
Regulatory uncertainty	No harmonized global standard for AI PV validation; jurisdiction variability	Moderate–High	ICH-facilitated global AI PV guidance; bilateral FDA-EMA AI framework harmonization	(Deutsch et al., 2026, p. 22)
Organizational resistance	Cultural reluctance to trust AI over experienced PV scientists	Moderate	Hybrid AI-human workflow design; PV scientist upskilling programs; change management	(Zemplényi et al., 2023, p. 5)
Cybersecurity risks	AI PV systems as high-value targets for adversarial manipulation	Moderate	Adversarial robustness testing; secure AI deployment architecture; penetration testing	(Yang et al., 2025, p. 12)

therapeutic area idioms. A constant challenge for the operation of an AI model is model drift—the erosion of its accuracy as the statistical characteristics of the input data change over time. PV data distributions are constantly evolving due to prescribing trends, new therapeutic classes entering the market, and reporting trends driven by safety communications and regulatory activity. The performance of static ML models trained on historical data from FAERS or EudraVigilance can be

significantly affected if they are not systematically retrained (Connor et al., 2022, p. 1; Martin et al., 2022, p. 546). Production-grade AI PV systems require continuous model monitoring frameworks, drift-detection algorithms, and automated retraining triggers, which can significantly increase infrastructure complexity. The reproducibility of AI research in PV has been subjected to critical scrutiny. Such a lack of reproducibility makes it difficult to critically evaluate, improve, and regulate published AI methods. Systemic correctives are recommended: TRIPOD-AI reporting standards, open-science data-sharing principles, and mandatory pre-registration of AI validation studies (Collins et al., 2024). The costs and technical expertise needed for infrastructure are major barriers to implementation, especially for small and medium-sized pharmaceutical companies and regulatory agencies in resource-poor countries (Palatty, Sacheendran and Jayachandran, 2024, p. 19). This barrier is partially alleviated by the development of scalable, cloud-based AI PV services provided by CROs and specialised PV technology companies; however, vendor dependency and data governance challenges remain. While the current state of practice is not fully implemented, there is a need for standardised APIs and HL7 FHIR-compliant data exchange architectures for enable interoperability among AI systems across different enterprise IT environments, regulatory submission platforms, and international safety databases.

9. FUTURE DIRECTIONS

AI's fusion with the new digital health technologies is poised to redefine pharmacovigilance in the next ten years. Precision pharmacovigilance—combining genomic, proteomic, metabolomic, microbiome, and real-world clinical data within AI analytical frameworks—will enable individual-level ADR risk prediction and mechanistically stratified signal characterisation, which are not possible with current population-level ADR surveillance (Giacon and Terrazzino, 2025; Zack et al., 2025). This paradigm aligns with the overall goals of precision medicine and positions PV as a core part of the therapeutic decision-making process rather than a regulatory afterthought (Chandana, 2023; Silva et al., 2024, p. 758). Federated learning (FL) architectures are a key new technical approach for collaborative AI model development in PV, while maintaining patient data sovereignty (Crisafulli et al., 2024, p. 8; Horst et al., 2025). In FL, model parameters rather than raw data are shared between participating institutions, enabling the development of ML models trained effectively on distributed datasets worldwide without centralising sensitive health data (Oldenhof et al., 2023, p. 15576; Horst et al., 2025). Federated approaches, such as MELLODDY (Machine Learning Ledger Orchestration for Drug Discovery), have already been shown to work in the context of pharmaceutical AI, as well as the FL architectures being piloted for distributed PV analytics based on EHRs in the Sentinel network and the European health data infrastructure (Ahire et al., 2024, p. 30; Zhao et al., 2025, p. 10).

Digital twin technology, which involves computational models of individual patients derived from longitudinal multimodal data, offers a revolutionary approach to simulating ADR in the future (Chande, Pharande and Karodi, 2025; Li et al., 2025). Patient-specific digital twins can be virtually exposed to proposed therapeutic interventions, and idiosyncratic drug responses can be predicted in silico prior to clinical administration (Björnsson et al., 2019). Although the current use of digital twins in clinical pharmacology is limited to research, ongoing clinical validation will enable their use as valuable tools for precision pharmacovigilance in polypharmacy patients and other complex patient groups with rare genetic risk factors (Chande, Pharande and Karodi, 2025; Li et al., 2025). Autonomous pharmacovigilance systems, which can process the entire ICSR workflow, from ICSR processing to signal detection, signal evaluation, and regulatory reporting, are a significant goal of AI integration in PV (Kumar et al., 2025). Immediate realisation of such a vision is the use of AI for autonomous monitoring of literature, automated generation of signal notification, and intelligent work queue management for PV case processing centres (Kumar et al., 2025). Achieving full autonomy will involve validated, explainable AI systems operating within regulatory-approved frameworks, and human oversight will be limited to exception management and complex benefit-risk deliberation (Shamim et al., 2024; Nestorovska-Gjoshevska and Ancevska-Netkovska, 2025).

The combination of blockchain and AI-powered PV systems could address issues of data integrity, audit trails, and multi-stakeholder trust. Immutable distributed ledgers for submitting ADR reports, signal detection events, and regulatory decisions provide tamper-evident provenance records for regulatory inspection and scientific reproducibility (Anichukwueze, Osuji and Oguntegbe, 2021). Although blockchain in PV is still in its early stages (Tripathi, Saini and Mishra, 2024), the synergy between blockchain and AI analytics, coupled with interoperable health data standards, offers a promising framework for future PV systems worldwide.

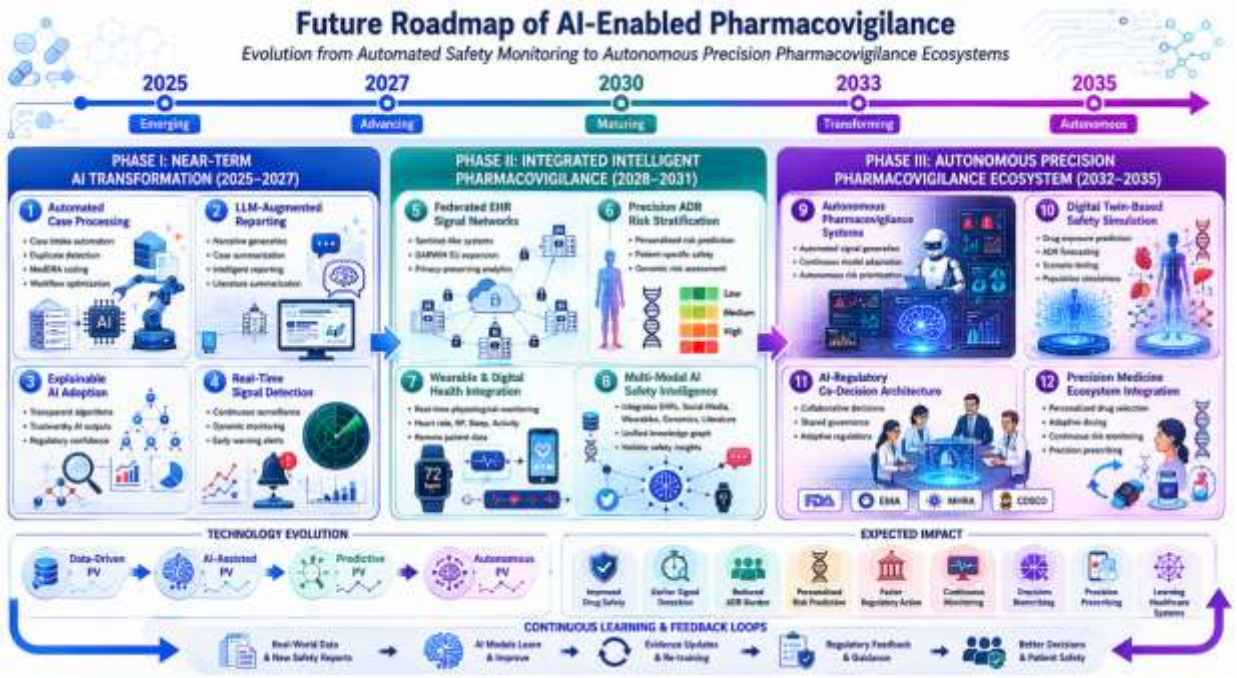

Figure 4. Future roadmap of AI-enabled pharmacovigilance.

The roadmap illustrates the anticipated evolution of pharmacovigilance from automated case processing and LLM-assisted reporting in the near term, through federated EHR signal networks, wearable integration, and precision adverse drug reaction risk stratification in the mid-term, toward autonomous pharmacovigilance systems incorporating digital twin–based safety simulations and AI-regulatory co-decision architectures. Collectively, these advances are expected to establish continuously learning precision medicine ecosystems capable of proactive, individualized, and predictive drug safety management.

10. Conclusion

The evolution of pharmacovigilance (PV) over the last 60 years has been maturing from reactive anecdotal reporting, triggered by drug safety violations, to a more systematized approach of signal science, based on databases. AI is a paradigm shift in this evolution, changing the way PV is done, how much and how fast. AI technologies are already providing measurable improvements in all of the drug safety science's main functions, with convergent clarity. Signal detection sensitivity and specificity are enhanced by ML-supported disproportionality analysis, graph neural network-based pharmacological contextual-isation and NLP-powered incorporation of previously unrecognized signals from social media and EHRs. AI-driven ICSR triage, automated coding and duplicate detection have revolutionised case processing efficiency, the operational backbone of any PV system, freeing up expert PV scientists to focus on more challenging safety interpretation tasks that require human expertise. Genomic, phenotypic, and pharmacological information is now being used in ADR prediction models, which will have a significant impact on preventable harm reduction at the individual patient level in the future. LLMs and generative AI are poised to transform PV processes, offering tremendous potential and challenges. The ability to automatically produce narrative case summaries, triage scientific literature at scale, and help build benefit-risk reports is a true efficiency multiplier for the PV. But the hallucination issue, where AI creates believable yet inaccurate content, requires human supervision in any PV workflow that uses AI to create safety-critical content. The validation studies, the sophistication of retrieval augmentation strategies, and the regulatory frameworks governing the use of AI in PV documentation will shape the future deployment architecture of LLMs in PV. The FDA's predetermined change control plan framework, EMA's Big Data and AI regulatory strategy, WHO's AI in health principles and the EU AI Act, all provide a governance environment that is truly enabling; acknowledging the transformative power of AI, but setting up the necessary safeguards to prevent patient harm from poorly validated systems. The task for the PV community is to make these frameworks a reality, with validated, transparent and continuously monitored AI deployments that satisfy the twin requirements of analytical performance and regulatory acceptability. Importantly, the transformative potential of AI in PV will only be achieved if the quality, representativeness, and equitable properties of the training data are continually considered. Training on biased reporting databases will lead to the reproduction and potential magnification of disparities in ADR detection by demographics, therapeutic classes, and geographic areas. These issues are not ancillary but fundamental to good practice in AI PV. The next generation of drug safety science will be defined by the challenge and opportunity of integrating precision PV capabilities enabled by federated learning architectures, digital biomarker streams, pharmacogenomic risk stratification, and digital twin simulation into the operational infrastructure of global regulatory databases. The dream of an independent, self-learning PV system that takes into account signals from spontaneous reports, EHRs, wearables, genome data, social media, and scientific publications, and builds a single, dynamically updated picture

of the real-world safety profile of each medicine, is no longer a distant scientific fantasy. In the end, the purpose of pharmacovigilance is to safeguard patients from avoidable harm and to keep the benefit-risk equation of medicines in favour of the benefits during the entire market life cycle of a medicine, which is exactly what AI technologies are best suited to do. This potential can only be realized through a concerted effort by pharmaceutical scientists, regulators, clinicians, informaticists, ethicists and patient advocates to create, validate, and implement AI systems that are not only technically capable, but also trustworthy. AI-enhanced PV will be one of the most significant uses of AI in the human health care – a combo of computer science and science, in the service of patients who rely on the medications for their wellbeing.

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