

# Unveiling the Signal: Next Generation Approaches to Drug Safety Surveillance

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## ABSTRACT:

The detection of adverse drug reactions (ADRs) remains a cornerstone of pharmacovigilance, yet traditional surveillance methods often struggle to keep pace with the complexity and speed of modern healthcare systems. This paper explores emerging, data-driven strategies for drug safety surveillance, emphasizing the integration of real-world evidence (RWE), machine learning algorithms, and advanced signal detection methods. These next-generation approaches leverage electronic health records, social media data, and global pharmacovigilance databases to identify safety signals earlier and more accurately than conventional techniques. We discuss the strengths and limitations of these technologies, regulatory considerations, and the need for transparency and explainability in algorithmic decision-making. By showcasing recent case studies and collaborative initiatives, we highlight the transformative potential of artificial intelligence and big data in reshaping drug safety monitoring and improving public health outcomes.

**Keywords-** Pharmacovigilance ,Adverse drug, reaction, signal detection Mchine learning .

## I. INTRODUCTION

Drug safety surveillance, a cornerstone of public health, has long depended on post-market monitoring systems such as the U.S. Food and Drug Administration's (FDA) MedWatch and the European Medicines Agency's (EMA) EudraVigilance. These systems, which rely heavily on spontaneous reporting from healthcare professionals and patients, have played a vital role in identifying adverse drug reactions (ADRs) after medications reach the market. However, as medical treatments grow more complex—encompassing biologics, gene therapies, and personalized medicine—traditional pharmacovigilance methods are no longer sufficient on their own.

(AI), machine learning (ML), and real-time analytics are transforming how safety signals

are detected, evaluated, and acted upon. Furthermore, the integration of real-world data (RWD)—sourced from electronic health records (EHRs), social media platforms, wearable devices, and mobile health applications—is enabling earlier and more accurate identification of potential safety risks.

At the heart of this transformation lies the concept of “unveiling the signal”: the proactive identification of subtle patterns and warning signs that may indicate emerging drug-safety risks. Recognizing the early cues that precede adverse outcomes and responding before widespread harm occurs.

This paper explores the evolution related risks. In a highly connected and data-saturated world, detecting these signals involves discerning meaningful information from vast noise—of drug safety surveillance in the era of digital health and advanced analytics. It examines the technologies, data sources, and methodologies driving this change, while addressing the challenges and opportunities they present. By embracing next-generation surveillance strategies, regulatory agencies, healthcare providers, and pharmaceutical companies can enhance patient protection and improve public health outcomes more effectively than ever before.

## Key Aspects of Next-Generation Drug Safety Surveillance

Next-generation surveillance harnesses powerful technologies and collaborative strategies to detect and manage adverse drug reactions (ADRs) with greater precision and speed. Key developments include:

**Harnessing Big Data & AI:** Leveraging large, diverse datasets and machine learning enables rapid detection of hidden safety signals.

**Real-Time Monitoring:** Advanced tools now allow near-instantaneous surveillance and response to emerging risks.

**Enhanced Epidemiology:** Improved cohort studies and global health data access support more accurate, population-specific risk assessments.

**Data Sources:** Combining clinical trial data, spontaneous reports, and real-world evidence provides a fuller safety profile of drugs.

**Patient-Centered Approaches:** Crowdsourcing and patient-reported outcomes add valuable insights often missed in clinical settings.

**Anticipatory & Predictive Analytics:** These tools forecast potential ADRs before they become widespread, supporting proactive safety measures

### Role of Next-Generation Drug Safety Surveillance

Next-generation approaches are revolutionizing drug safety surveillance by introducing continuous, data-driven, and patient-centered methodologies. These innovations aim to detect and prevent adverse drug reactions (ADRs) more effectively, ensuring better protection for patients. Key roles include:

#### 1. Continuous Data Surveillance:

Real-time monitoring of adverse events through large pharmacovigilance databases like FAERS and EudraVigilance.

Advanced analysis of electronic health records (EHRs) using machine learning and natural language processing to detect post-market safety signals.

#### 2. Sophisticated Data Analytics:

Machine learning and advanced statistical tools enhance signal detection.

Predictive analytics help forecast ADRs before they occur on a larger scale.

#### 1. AI and Machine Learning Applications:

Automation of adverse event case evaluation improves efficiency and accuracy.

Pattern recognition algorithms uncover early safety trends and emerging risks.

##### 1. Real-World Evidence (RWE):

- Observational data from sources like insurance claims and patient registries offer insights into real-world drug use.

### Goals of Next-Generation Pharmacovigilance

Next-generation pharmacovigilance focuses on enhancing the speed, accuracy, and personalization of drug safety monitoring through advanced technology and diverse data sources. Its key aims include:

#### 1. Accelerating Signal Detection

- Quickly identify safety concerns after drug launch.
- Reduce delays in recognizing emerging risks to protect patients sooner.

#### 2. Increasing Detection Accuracy

- Improve true signal identification.
- Reduce false alarms, ensuring focus on real safety threats.

#### 3. Utilizing Multiple Data Streams

- Integrate data from EHRs, social media, wearables, patient groups, insurance, and genetics.
- Gain a broader, more detailed understanding of drug effects across varied populations.

#### 4. Harnessing AI and Machine Learning

- Automate pattern recognition for faster, smarter signal detection.
- Continuously refine systems for greater long-term accuracy.

#### 5. Enabling Personalized Risk Assessment

- Tailor safety monitoring to individual factors like genetics, age, and health conditions.
- Support more precise, patient-specific pharmacovigilance.

### Traditional Drug Safety Surveillance

#### Purpose:

Ensure the safe and effective use of medications by identifying, evaluating, and preventing adverse drug reactions (ADRs).

#### Main Methods:

##### 1. Spontaneous Reporting Systems

- **Definition:** Voluntary ADR reports from patients, providers, or manufacturers.
- **Pros:** Easy, broad reach.
- **Cons:** Underreporting, bias, limited detail.

##### 2. Cohort Event Monitoring (CEM)

- **Definition:** Follows a group of drug users over time.
- **Pros:** Real-world, detailed safety data.
- **Cons:** Resource- and time-intensive.

##### 3. Case-Control Studies

- **Definition:** Compares drug exposure in patients with and without ADRs.
- **Pros:** Good for rare ADRs.

- **Cons:** Recall bias, difficult control selection.
- 4. **Prescription Event Monitoring (PEM)**
- **Definition:** Tracks ADR trends through prescription data.
- **Pros:** Detects widespread safety signals.
- **Cons:** Weak at identifying delayed effects.
- 5. **Active Surveillance**
- **Definition:** Proactive ADR tracking (e.g., EHRs, follow-ups).
- **Pros:** More accurate than passive systems.
- **Cons:** High cost and complexity.
- 6. **Data Mining & Signal Detection**
- **Definition:** Uses statistics to find unexpected ADRs in large databases.
- **Pros:** Scalable, fast.
- **Cons:** Risk of false signals.
- 7. **Risk Management Plans (RMPs)**
- **Definition:** Regulatory plans by manufacturers to manage drug risks.
- **Components:** Risk identification, minimization, and communication.

#### Adverse drug reaction

Adverse Drug Reaction Reporting System (ADRS) is a critical component of pharmacovigilance, aimed at collecting, evaluating, and monitoring reports of drug-related side effects to ensure medication safety. It relies on multiple **reporting channels** (healthcare providers, patients, pharmaceutical companies) and includes detailed data on drug reactions, patient demographics, and outcomes. Key systems like **MedWatch (USA)**, **EudraVigilance (EU)**, and **theyellowCardScheme (UK)** support this process.

Modern pharmacovigilance is evolving by incorporating **big data analytics**, **real-world evidence**, **AI**, and **electronic health records (EHRs)** to enhance traditional drug monitoring methods. However, there are significant challenges, including **biases in data reporting**, **inconsistent data standards**, and **privacy concerns**.

#### Limitation

These limitations highlight the existing surveillance models:

#### 1. Privacy Concerns:

Surveillance systems often collect vast amounts of personal data, risking privacy violations and potential misuse of information beyond its intended scope.

#### 2. Data Quality Issues:

AI-driven systems can be inaccurate, leading to false positives or missed threats. Incomplete or inconsistent data further hampers system reliability.

#### 3. Scalability Challenges:

Scaling surveillance requires significant resources and may lack flexibility to adapt quickly to new threats or changing environments.

#### 4. Ethical and Legal Issues:

Surveillance can conflict with legal regulations like GDPR and poses moral dilemmas, particularly in regions with authoritarian governance.

#### 5. Technological Limitations:

These systems can be vulnerable to cyberattacks and are often limited by the capabilities of current hardware and software.

#### 6. Bias and Overreliance on Technology:

AI surveillance can inherit biases from training data, leading to discrimination, and excessive dependence on technology may overlook valuable human insight.

#### Advancing Drug Safety Surveillance

The field of **drug safety surveillance** is undergoing major transformation, driven by new technologies and expansive data sources aimed at improving the detection and prevention of **adverse drug reactions (ADRs)**. Key advancements include:

#### 1. Real-World Data (RWD) & Evidence (RWE):

Leveraging data from EHRs, insurance claims, registries, and even social media to identify safety issues in real-time and across diverse populations.

#### 2. Pharmacovigilance 4.0:

Integrating **AI and machine learning (ML)** for trend analysis and risk prediction, and using **natural language processing (NLP)** to extract insights from unstructured clinical and scientific data.

#### 3. Big Data Analytics:

Utilizing vast datasets to detect rare ADRs and emerging signals, and applying **predictive analytics** to anticipate risks before they escalate.

#### 4. **Advanced Signal Detection Tools:**

Employing methods like **Bayesian data mining** and **disproportionality analysis** to automate and prioritize safety signal assessment.

#### 5. **Personalized Medicine & Pharmacogenomics:**

Exploring genetic variations to predict individual drug responses and prevent adverse interactions based on genetic profiles.

#### 6. **Global Surveillance Networks:**

Creating international data-sharing platforms to enhance the speed and scope of safety monitoring among regulators and healthcare providers.

#### 7. **Patient Involvement:**

Encouraging patient-reported outcomes (PROs) and using **crowdsourced data** to detect ADRs from the user perspective.

#### 8. **Blockchain Technology:**

Applying blockchain for secure, transparent, and tamper-proof pharmacovigilance data handling.

#### **Impact of AI & ML on Pharmacovigilance:**

AI and ML are transforming pharmacovigilance by enabling:

- **Faster and smarter signal detection** from large, diverse data sources.
- **More accurate risk evaluations** by identifying subtle patterns and predicting future safety concerns

#### **Data analytics is vital in strengthening drug safety by modernizing pharmacovigilance efforts.**

It enables the early identification, evaluation, and prevention of adverse drug reactions (ADRs) through the following essential components:

#### **Real-Time Monitoring & Early Detection Systems**

- **Social Media & Online Health Communities:** Detect ADRs by analyzing content shared by users on platforms like Twitter and health forums.
- **Electronic Health Records (EHRs):** Monitor patient health outcomes and identify patterns associated with medication use.

#### **Risk Prediction Through Advanced Modeling**

- **Machine Learning Techniques:** Predict potential safety concerns by analyzing both historical and real-time health data.
- **Risk Stratification:** Leverage genetic, demographic, and clinical information to determine patient groups at greater risk of adverse effects.

#### **Detection of Safety Signals via Real-World Evidence (RWE)**

- **RWE**, sourced from real-world data (RWD) such as EHRs, insurance data, patient registries, wearable devices, and social platforms, provides critical insights into drug effectiveness and safety in everyday clinical settings.

#### **Automation in Drug Safety Monitoring**

- **Natural Language Processing (NLP):** Extracts valuable data from unstructured sources like clinical documentation, scientific literature, and online discussions.
- **Automated Reporting Systems:** Streamline the generation of required safety reports for health authorities.

#### **Improving Regulatory Oversight and Compliance**

- **Faster Reporting Capabilities:** Enhance responsiveness to emerging safety concerns for regulatory bodies such as the FDA and EMA.
- **Integrated Safety Data:** Combine information from clinical trials, post-market surveillance, and patient registries to form a complete picture of drug safety.

#### **Regulatory Acceptance**

- For AI-based pharmacovigilance tools to be broadly implemented, they must adhere to rigorous regulatory criteria ensuring their **dependability, safety.**

#### **The Role of Real-World Evidence (RWE) in Drug Safety Monitoring**

Real-World Evidence (RWE), derived from Real-World Data (RWD) such as electronic health records, insurance claims, and wearable devices, plays a vital role in monitoring drug safety beyond controlled clinical trials.

### Key Contributions of RWE to Drug Safety:

- 1. Early Detection of Adverse Drug Reactions (ADRs):**
  - Identifies rare or delayed side effects, often missed in clinical trials.
  - Example: Blood clot risks linked to certain COVID-19 vaccines.
- 2. Safety Signal Detection and Risk Evaluation:**
  - Uses tools like AI, Bayesian analysis, and pharmacovigilance systems (e.g., FAERS, EudraVigilance) to uncover safety concerns.
- 3. Post-Market Surveillance (Phase IV Studies):**
  - Monitors drug performance across diverse populations in real-life settings.
  - Captures data on adherence, interactions, and subgroup-specific risks.
- 4. Benefit-Risk Analysis:**
  - Compares real-world drug efficacy against potential harms to support decisions on labeling, mitigation strategies, or market withdrawal.
- 5. Regulatory Support:**
  - Agencies like the FDA and EMA use RWE to inform approvals, warnings, and regulatory updates.
- 6. Focus on Special Populations:**
  - Enables safety tracking in underrepresented groups like the elderly or pregnant women.

### Challenges in RWE Use:

- Data quality issues (inaccuracy, incompleteness)
- Confounding variables and bias
- Difficulty in proving causality
- Privacy and confidentiality concerns

### Innovations and Applications:

- **AI/ML & NLP Integration:** Enhances signal detection and analysis of unstructured data (e.g., clinical notes).
- **Pharmacovigilance Enhancement:** Enables rapid issue recognition and early detection from diverse data streams.
- **Comprehensive Risk Management:** Provides insights across varied populations for tailored risk assessment.
- **Post-Marketing Surveillance:** Tracks long-term safety and compares drug effectiveness in real-world settings.
- **Personalized Medicine:** Incorporates genetic data to refine drug response predictions and identify high-risk groups.

- **Regulatory Evolution:** Supports flexible, data-driven regulatory strategies for timely safety decisions.
- **Global Collaboration:** Encourages international data sharing for stronger worldwide safety networks.

### Data Source and Integration for Signal Detection

Signal detection is vital in fields like telecommunications, healthcare, finance, and environmental monitoring, where it involves identifying important signals within noisy or irrelevant data. The effectiveness of signal detection depends significantly on both the quality of the data and how well it's integrated.

### Types of Data Sources:

- 1. Sensor-Driven Data Sources:**
  - Physical Sensors: Measure real-world conditions (e.g., temperature, pressure, motion).
  - Biological Sensors: Capture physiological signals like EEG and ECG.
  - Environmental Sensors: Monitor air quality, seismic activity, and weather conditions.
  - Data: Support geospatial signal analysis, particularly in environmental and defense applications.
- 2. Challenges in Data Integration for Signal Digital and Streaming Data Sources:**
  - Network Traffic: Used in cybersecurity for detecting anomalies.
  - Financial Market Data: Helps identify patterns in high-frequency trading.
  - IoT Devices: Continuously stream data for real-time analysis.
- 3. Historical and External Data Sources:**
  - Databases and Archives: Provide historical context for training detection models.

### Detection:

- 1. Data Diversity** – Integrating varied data formats and types is complex.
- 2. Real-Time Processing Needs** – Rapid data processing is needed for timely signal detection.
- 3. Quality Assurance** – Inconsistent or noisy data can reduce accuracy.
- 4. Scalability** – Large-scale, multi-source data requires strong infrastructure.

### Real-World Evidence (RWE):

RWE is clinical insight derived from Real-World Data (RWD) collected in routine healthcare

(e.g., EHRs, claims, registries, wearables, social media).

#### Key Uses of RWE:

1. **Regulatory Decisions** – Used by agencies like FDA/EMA for drug approvals, indication expansion, and post-market safety (e.g., Eliquis).
2. **Health Technology Assessment (HTA)** – Evaluates treatment cost-effectiveness and guides policy and insurance coverage.
3. **Drug Development & Trials** – Speeds up trials, especially for rare diseases, and streamlines participant recruitment.
4. **Pharmacovigilance** – Enables long-term drug safety monitoring beyond controlled trial settings.

#### Electronic health record

Electronic Health Records (EHRs) are digital systems used by healthcare providers to manage patient information, including demographics, medical history, diagnoses, medications, lab results, and treatment plans. EHRs enhance care coordination by enabling information sharing across providers and support clinical decisions by flagging risks like drug interactions.

A major challenge in EHR systems is **data consistency**, as variations in data formats and sources can complicate analysis.

#### Genomic Data and Personalized Medicine:

Genomic data, derived from DNA sequencing, provides insight into genetic variations that influence an individual's response to diseases and treatments. Personalized (or precision) medicine leverages this data to:

- Predict disease risk,
- Optimize drug effectiveness and minimize side effects, and
- Guide preventive care strategies.

The future of genomics and personalized medicine looks promising due to technological advancements. Genomic testing is becoming more affordable and accurate, leading to wider clinical use. The integration of AI and machine learning will enhance the analysis of complex genomic data, improving disease risk prediction, drug discovery, and personalized treatments. Additionally, gene editing tools like CRISPR may transform genetic disease treatment by correcting DNA mutations directly.

#### Advanced Signal Detection Techniques

Signal detection is fundamental in technologies like communications, radar, biomedical systems, and sensors. As these systems face increasing noise, variability, and data volume, advanced detection methods are essential. These techniques go beyond traditional thresholding and matched filtering, offering improved accuracy through:

- **Statistical inference** (e.g., Bayesian methods, Neyman-Pearson criterion)
- **Adaptive filtering** (e.g., Kalman filter, LMS, RLS)
- **Machine learning and AI** (e.g., neural networks, SVMs, CNNs)
- **Cognitive spectrum sensing**, particularly in dynamic frequency environments
- **Time-frequency analysis** using tools like wavelet transforms

These methods enhance signal identification in complex environments, with applications spanning wireless communication, biomedical diagnostics, and environmental monitoring.

#### Natural Language Processing in Drug Safety

Natural Language Processing (NLP) helps automate the analysis of large, unstructured healthcare texts to improve drug safety monitoring (pharmacovigilance). Traditional methods are manual and error-prone, while NLP enables real-time data processing from sources like EHRs, clinical notes, literature, and social media. Key applications include:

- **Adverse Event Detection:** Extracting drug-related adverse reactions from clinical documentation and reports
- **Automation of pharmacovigilance:** Enhancing speed, accuracy, and scale of drug safety surveillance

NLP is transforming drug safety by enabling earlier and more accurate identification of potential drug-related risks.

#### Benefits of NLP in Drug Safety

1. **Efficiency and Speed** – Rapidly processes large volumes of unstructured data to detect ADRs faster than manual methods.
2. **Improved Coverage** – Analyzes diverse data sources, including clinical notes and patient feedback, often missed in traditional systems.
3. **Scalability** – Handles growing volumes of data from various sources, supporting extensive drug safety monitoring.

4. **Cost-Effectiveness** – Automates data analysis, reducing manual workload and operational costs.
5. **Comprehensive Monitoring** – Enhances the depth and breadth of pharmacovigilance efforts.

#### Challenges and Limitations of NLP in Drug Safety

- **Data Quality Issues** – Poor data quality reduces NLP effectiveness.
- **Complex Medical Terminology** – Ambiguity and context-dependence of medical terms can challenge NLP accuracy.
- **System Integration** – Effective implementation requires seamless integration with existing drug safety infrastructure.

#### Predictive Analytics in ADR Detection

- **Proactive Risk Identification** – Unlike reactive traditional methods, predictive analytics can forecast ADR risks before widespread issues arise.
- **Enhanced Monitoring** – Integrating predictive models into pharmacovigilance systems improves early detection and prevention of adverse events.

#### Key Techniques in Predictive Analytics

1. **Historical Data Use** – Leverages data from EHRs, trials, surveillance systems, and claims to identify high-risk populations.
2. **Machine Learning Methods:**
  - **Decision Trees** – Classify risk based on patient factors.
  - **Random Forests** – Improve accuracy using multiple decision trees.
  - **Support Vector Machines (SVM)** – Distinguish ADRs from non-ADRs.
  - **Neural Networks** – Detect complex patterns in large-scale datasets.

#### Applications and Challenges of Predictive Analytics in ADR Detection

##### Applications:

1. **Early Detection of ADRs:** Predictive models can identify early warning signs in patient data, allowing timely interventions before adverse drug reactions (ADRs) become serious.
2. **Risk Stratification and Personalized Medicine:** Analytics helps tailor treatments based on individual risk profiles derived from

medical history, genetics, and drug use, improving safety and efficacy.

3. **Signal Detection and Prioritization:** Large datasets are analyzed to uncover subtle or rare ADR patterns, especially in specific subpopulations, enhancing regulatory oversight.
4. **Drug Interaction Analysis:** Predictive tools detect harmful drug-drug interactions by analyzing prescribing patterns and clinical trial data, preventing adverse outcomes.
5. **Long-term Safety Monitoring:** Post-market surveillance uses predictive models to identify ADRs that arise over time or in broader patient groups than those in clinical trials.

##### Challenges:

1. **Data Quality and Completeness:** Poor or biased data can lead to inaccurate predictions and weaken the reliability of ADR detection.
2. **Complex Drug Interactions:** Modeling interactions among multiple factors (e.g., drugs, genetics, environment) is difficult and requires advanced algorithms.
3. **Integration with Existing Infrastructure:** Incorporating predictive analytics into current healthcare systems demands robust data pipelines, platform compatibility, and adherence to privacy and regulatory standards.

## II. CONCLUSION

The article discusses the transformation of drug safety surveillance through the integration of advanced technologies such as artificial intelligence (AI), machine learning, and real-world data. Traditional pharmacovigilance methods are being enhanced by these innovations to enable faster and more accurate detection of adverse drug reactions. The shift toward real-time, data-driven monitoring emphasizes cross-disciplinary collaboration and the ethical use of data. Key to this evolution are standardized frameworks, stakeholder cooperation, and the continuous adaptation of safety systems. Overall, these advancements aim to make pharmacovigilance more proactive, personalized, and effective in improving patient safety and public health outcome.

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