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Role of Real-World Evidence in Pharmacovigilance: From Signal Detection to Regulatory Decision-Making – A Narrative review

Dr. Sobana Tamilselvan[1], S. Lavanya[2]

[1]Associate Professor, Pachamuthu College of Pharmacy, Dharmapuri, Tamil Nadu – 636705, Affiliated to The Tamil Nadu Dr. MGR Medical University, Chennai.

[2]B. Pharm, Pachamuthu College of Pharmacy, Dharmapuri, Tamil Nadu – 636705, Affiliated to The Tamil Nadu Dr. MGR Medical University, Chennai.

*Corresponding Author

Dr. Sobana Tamilselvan,

Associate Professor

Pachamuthu College of Pharmacy

Krishnagiri Main Road, Dharmapuri,

Tamil Nadu- 636 705.

Email ID: sobanaselvan@gmail.com

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Abstract

Pharmacovigilance plays an important role in ensuring the safety of medicines after they are introduced into clinical practice. Although randomized controlled trials are essential for evaluating the safety and efficacy of drugs before approval, they often fail to identify rare or delayed adverse drug reactions because they involve limited patient populations and are conducted under controlled conditions. Real-world evidence (RWE), generated from sources such as electronic health records, patient registries, insurance claims databases, spontaneous adverse drug reaction reporting systems, and digital health technologies, provides valuable information on the safety and effectiveness of medicines in routine clinical settings. In recent years, RWE has become an important component of pharmacovigilance by supporting early safety signal detection, risk assessment, regulatory decision-making, and continuous evaluation of marketed medicines. This review discusses the role of real-world evidence in pharmacovigilance, the major sources of real-world data, important drug withdrawal case studies, current challenges, and future developments, including the application of artificial intelligence and big data in drug safety monitoring

Introduction

Pharmacovigilance refers to the science and practice of detecting, assessing, understanding, and preventing adverse drug reactions (ADRs) and other medicine-related problems. It plays an important role in protecting patient safety by continuously monitoring medicines after they are approved for use. Despite careful evaluation during clinical trials, adverse drug reactions continue to contribute to significant morbidity and mortality worldwide, highlighting the need for effective post-marketing surveillance. [1,2]

Randomized controlled trials (RCTs) are considered the standard method for assessing the safety and efficacy of medicines before they reach the market. However, these studies are usually conducted in controlled environments with a limited number of participants and relatively short follow-up periods. As a result, uncommon or delayed adverse drug reactions may remain undetected until the medicine is used by a larger and more diverse population [3–5].

To address these limitations, real-world evidence (RWE) has become an important part of modern pharmacovigilance. It is generated from real-world data collected through electronic health records, patient registries, insurance claims databases, spontaneous adverse drug reaction reporting systems, and other healthcare sources. These data provide valuable information on the long-term safety, effectiveness, and utilization of medicines in routine clinical practice. Regulatory agencies such as the FDA, EMA, and WHO increasingly encourage the use of real-world evidence to strengthen pharmacovigilance activities and support evidence-based healthcare decisions [6–9].

Methodology

A narrative review was conducted using published literature from WHO, FDA, EMA, peer-reviewed journals, and pharmacovigilance databases. Information on sources of RWD, regulatory applications, drug withdrawal case studies, and future developments in RWE was analysed**.**

1. Overview of Real-World Evidence

Real-world evidence (RWE) refers to clinical evidence obtained by analysing real-world data (RWD) collected during routine healthcare practice. Unlike data generated from randomized controlled trials, RWE reflects how medicines are used in everyday clinical settings and provides information on their benefits and potential risks in a broader patient population [10].

Characteristics of Real-World Evidence:

Real-world evidence has several important characteristics that make it valuable in pharmacovigilance. It:

- Is generated from routine clinical practice.

- Includes patients from different age groups and medical conditions.
- Supports long-term follow-up of medicine use.
- Contributes to post-marketing surveillance activities.
- Reflects real-world clinical practice and treatment patterns. [11].

Sources of Real-World Data:

Real-world data can be collected from a variety of healthcare sources, including:

- Electronic health records (EHRs)
- Insurance claims databases
- Patient registries
- Spontaneous adverse drug reaction (ADR) reporting systems
- Pharmacy databases
- Mobile health applications
- Wearable devices [12]

Importance of Real-World Evidence:

Real-world evidence plays an important role in improving medicine safety and patient care. It helps to:

- Detect rare adverse drug reactions.
- Assess the effectiveness of medicines in routine clinical practice.
- Evaluate drug safety in special patient populations.
- Support regulatory and healthcare decision-making.
- Improve overall patient outcomes through continuous safety monitoring [13].

2. **Importance of Real-World Evidence in Detecting Rare and Serious ADRs**

Adverse Drug Reactions

Randomized controlled trials (RCTs) are essential for evaluating the safety and efficacy of medicines before approval. However, these studies usually involve a limited number of participants and have relatively short follow-up periods. Because of these limitations, uncommon or delayed adverse drug reactions (ADRs) may not be identified until the medicine is widely used in routine clinical practice. Real-world evidence (RWE) helps overcome this limitation by providing safety information from large and diverse patient populations over extended periods [14].

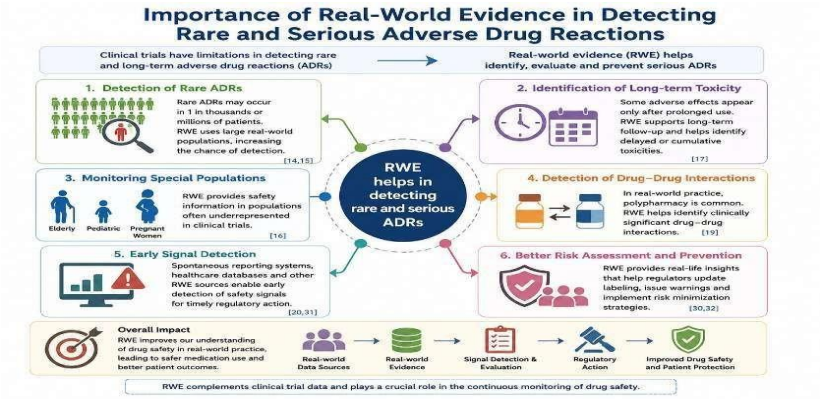

Figure 1: Importance of RWE in detecting Rare and serious ADR

Detection of Rare Adverse Drug Reactions

One of the major advantages of RWE is its ability to identify rare adverse drug reactions that may not be observed during pre-marketing clinical trials. Continuous monitoring of medicines after approval allows healthcare professionals and regulatory agencies to detect new safety concerns at an early stage [15].

Example

Rofecoxib, a selective cyclooxygenase-2 (COX-2) inhibitor used for pain management, was later found to increase the risk of myocardial infarction and stroke. These serious cardiovascular adverse effects were identified through post-marketing surveillance and real-world studies, which eventually led to its withdrawal from the market [16].

Identification of Long-Term Toxicity

Certain adverse drug reactions develop only after prolonged use of a medicine. Real-world evidence supports long-term follow-up and helps identify delayed adverse effects and cumulative

toxicities that may not become apparent during clinical trials. [17]

Monitoring Special Populations

Many patient groups, such as pregnant women, children, older adults, and individuals with multiple comorbidities, are often underrepresented or excluded from clinical trials. Real-world evidence provides valuable information about the safety and effectiveness of medicines in these special populations, helping clinicians make informed treatment decisions [18].

Detection of Drug–Drug Interactions

Polypharmacy is common in routine clinical practice, especially among elderly patients and those with chronic diseases. Real-world data help identify clinically important drug–drug interactions and medication-related problems that may not be recognised during pre-marketing studies [19].

Early Safety Signal Detection

Spontaneous adverse drug reaction reporting systems, national pharmacovigilance databases, and other real-world data sources support the early identification of safety signals. Prompt detection of these signals enables regulatory authorities to evaluate potential risks and implement appropriate measures to improve patient safety [20].

4. Sources of Real-World Evidence for Pharmacovigilance

Primary sources of real-world data, which include electronic health records, Health insurance claims and Billing Data, Patient Registries, Patient-Generated Data(PGD) Social media and Online data, Pharmacy and Point-of-sale Data, Laboratory and Genomic Data, Data from Devices and

Monitoring Systems, and Public Databases and Government Sources as shown in the figure. [10,11]

Figure 2. Sources of Real-World Evidence (RWE)

4.1. Electronic Health Records (EHRs)

Electronic Health Records (EHRs) are digital patient records maintained by healthcare providers. They include demographic details, diagnoses, medications, laboratory results, clinical notes, and vital signs. EHRs provide comprehensive real-world clinical data that help evaluate disease patterns, treatment effectiveness, and patient outcomes. [11,12]

4.2. Health Insurance Claims and Billing Data

Health insurance claims databases contain information on inpatient and outpatient services, prescription claims, procedure codes, healthcare utilization, and associated costs. These databases are widely used to assess healthcare resource utilization, treatment patterns, and economic outcomes in large populations. [11,12]

4.3. Patient Registries

Patient registries systematically collect data on individuals with specific diseases or conditions over time. They provide valuable information on treatment patterns, long-term clinical outcomes, safety, and disease progression, supporting observational and post-marketing studies.[11]

4.4. Patient-Generated Data (PGD)

Patient-generated data are collected directly from patients through wearable devices, fitness trackers, mobile health applications, and patient-reported outcome measures. These data offer insights into symptoms, quality of life, treatment adherence, and daily health status.[20]

4.5. Social Media and Online Data

Social media platforms, online patient forums, and digital communities provide information on patient experiences, treatment satisfaction, adverse events, and public perceptions of healthcare interventions. These data can complement traditional data sources but require careful validation. [9,20]

4.6. Pharmacy and Point-of-Sale Data

Pharmacy databases record prescription refills, over-the-counter medication purchases, medication adherence, and drug utilization patterns. These data are useful for evaluating medication use and prescribing trends in routine clinical practice.[11]

4.7. Laboratory and Genomic Data

Laboratory test results, biobanks, genomic databases, omics data, and biomarker information provide biological evidence that supports disease diagnosis, precision medicine, and assessment of treatment response in real-world settings. [11,20]

4.8. Data from Devices and Monitoring Systems

Medical devices, implantable devices, wearable sensors, remote patient monitoring systems, imaging technologies, and home monitoring devices continuously generate health-related data. These sources enable real-time monitoring of patient health and disease management.[20]

4.9. Public Databases and Government Sources

Public databases maintained by government agencies include census data, vital statistics, disease surveillance records, public health databases, and environmental data. These datasets are essential for epidemiological research, population health studies, and healthcare policy development. [11,13]

Source of RWE	Key Data Collected
Electronic Health Records (EHRs)	Demographics, diagnoses, medications, laboratory results.
Health insurance claims	Healthcare utilization, procedure, and cost data.
Patient Registries	Disease-specific data, treatment outcomes.
Patient-generated data	Wearables, mobile apps, patient reported outcomes
Social Media and online data	Patient experiences, adverse events, public opinions
Pharmacy data	Prescription refills, medication adherence, drug utilization

Laboratory & Genomic data	Laboratory tests, biomarkers, genomic information
Devices & Monitoring systems	Wearables, remote monitoring, implantable devices
Public databases	Census, diseases surveillance, vital statistics

TABLE 1. Sources of Real-World Evidence (RWE) and their applications

5.Examples of Real Case Studies: Reasons for Drug Withdrawal

Table 2. Real-world case studies illustrating reasons for drug withdrawal and the role of pharmacovigilance.

S.no	Drug	Primary Indication	Reason for withdrawal	Year of Withdrawal
1	Thalidomide	Sedative; treatment of morning sickness	Severe Teratogenicity (birth defects)	1961
2	Rofecoxib	Pain and arthritis	Increased cardiovascular risk	2004
3	Cerivastatin	Hypercholesterolemia	Rhabdomyolysis and acute renal failure	2001
4	Cisapride	Gastroesophageal Reflux disease	QT prolongation and fatal cardiac arrhythmias	2000

5	Troglitazone	Type 2 diabetes mellitus	Severe hepatotoxicity	2000
6	Fenfluramine& Dexfenfluramine	Obesity	Valvular heart disease and pulmonary hypertension	1997
7	Terfenadine	Allergic disorders	Cardiotoxicity due to drug interactions	1998
8	Rosiglitazone	Type 2 diabetes mellitus	Cardiovascular complications	Restricted (2010)
9	Benoxaprofen	Arthritis	Hepatoxicity and photosensitivity	1982
10	Propoxyphene	Pain management	Fatal cardiac toxicity and overdose risk	2010

5.1 Thalidomide

Thalidomide was introduced in the late 1950s as a sedative and was also prescribed to relieve morning sickness in pregnant women. After its widespread use, thousands of babies were born with severe congenital abnormalities, particularly limb deformities known as phocomelia. These serious birth defects were identified through post-marketing reports, leading to the withdrawal of the drug in many countries. This tragic incident emphasized the need for strict drug safety monitoring, especially during pregnancy, and became a major milestone in the development of modern pharmacovigilance [16].

5.2 Rofecoxib

Rofecoxib, a selective cyclooxygenase-2 (COX-2) inhibitor, was widely prescribed for the treatment of pain and

inflammation. Although it showed good efficacy during clinical trials, post-marketing studies later revealed an increased risk of myocardial infarction and stroke among long-term users. Based on these findings, the medicine was withdrawn from the market in 2004. This case demonstrated the value of real-world evidence in identifying serious cardiovascular adverse effects that were not fully recognized before approval [15,17].

5.3 Cerivastatin

Cerivastatin was a lipid-lowering medicine belonging to the statin class. After its introduction into clinical practice, several cases of severe rhabdomyolysis and acute renal failure were reported, particularly when it was used together with gemfibrozil. Continuous safety monitoring confirmed that the benefits no longer outweighed the risks, resulting in its withdrawal from the market. This case highlighted the importance of monitoring drug–drug interactions and rare adverse reactions after marketing [19].

5.4 Cisapride

Cisapride was commonly used to treat gastroesophageal reflux disease and other gastrointestinal motility disorders. During post-marketing surveillance, reports showed that the medicine could prolong the QT interval and cause serious ventricular arrhythmias, including torsades de pointes, particularly when taken with medicines that inhibit CYP3A4. Owing to these life-threatening cardiac events, cisapride was withdrawn or its use was severely restricted in many countries. This case reinforced the importance of continuous pharmacovigilance and careful evaluation of medicine safety in routine clinical practice [19].

5.5 Troglitazone

Troglitazone was introduced as an oral antidiabetic medicine for the management of type 2 diabetes mellitus. Following its approval, several patients developed severe liver injury, including acute liver failure requiring liver transplantation. Evidence obtained from post-marketing surveillance confirmed the association between troglitazone and hepatotoxicity, leading to its withdrawal from the market. This case demonstrated the importance of continuous

monitoring of medicine safety even after regulatory approval [13].

5.6 Fenfluramine and Dexfenfluramine

Fenfluramine and dexfenfluramine were widely prescribed as appetite suppressants for the management of obesity. After they were introduced into routine clinical practice, post-marketing reports showed an increased risk of heart valve disorders and pulmonary hypertension. These serious adverse effects led to the withdrawal of both medicines from the market. This case demonstrated the importance of continuous safety monitoring in identifying rare but serious adverse drug reactions that were not evident during clinical trials [19].

5.7 Terfenadine

Terfenadine was an antihistamine commonly used to treat allergic conditions. During post-marketing surveillance, it was found to cause serious cardiac arrhythmias, especially when taken with medicines that inhibit the CYP3A4 enzyme. These interactions increased the risk of QT interval prolongation and torsades de pointes. Because safer alternatives became available, terfenadine was withdrawn from the market. This case highlighted the importance of monitoring drug–drug interactions through pharmacovigilance activities [19].

5.8 Rosiglitazone

Rosiglitazone was an oral antidiabetic medicine used in the treatment of type 2 diabetes mellitus. Although it was effective in improving glycaemic control, post-marketing studies suggested an increased risk of myocardial infarction and other cardiovascular events in some patients. These safety concerns resulted in major regulatory restrictions and withdrawal from several markets. The case emphasized the value of real-world evidence in evaluating the long-term cardiovascular safety of medicines [21,22].

5.9 Benoxaprofen

Benoxaprofen was a non-steroidal anti-inflammatory drug (NSAID) used to treat arthritis and other inflammatory disorders. Following its approval, reports of severe liver toxicity and photosensitivity reactions were received, particularly among elderly patients. These findings led to the withdrawal of the medicine from the

market. This case highlighted the importance of monitoring medicine safety in vulnerable patient groups after marketing [12].

5.10 Propoxyphene

Propoxyphene was an opioid analgesic prescribed for the relief of mild to moderate pain. Real-world safety data later showed that the medicine was associated with serious cardiac toxicity, including abnormal heart rhythms, especially when used at high doses or in overdose. As the risks were considered greater than the benefits, the medicine was withdrawn from many countries. This case demonstrated how post-marketing surveillance supports timely regulatory action to improve patient safety [23].

Importance of These Case Studies in Pharmacovigilance

These withdrawals demonstrated that:

- Rare adverse drug reactions may not appear during clinical trials. [5,6]
- Real-world evidence and post-marketing surveillance are essential for detecting long-term and rare toxicities. [3,4]
- Spontaneous adverse drug reaction reporting systems help identify safety signals early. [8,18]
- Pharmacovigilance protects public health by ensuring continuous monitoring of medicines after approval. [1,2]

Key Pharmacovigilance Lessons

- Continuous safety monitoring is necessary even after drug approval.
- Real-world data from hospitals, electronic health records, and ADR databases are valuable.
- Early signal detection can prevent morbidity and mortality. [19]

6. Refine safety profiles based on Real-world data.

Real-world data (RWD) plays an important role in improving the safety profile of medicines after they are approved for public use. Although randomized clinical trials are essential for evaluating the safety and efficacy of medicines before marketing, they are usually conducted in controlled settings with a limited number of participants and strict inclusion criteria. As a result,

uncommon or delayed adverse drug reactions may not be identified during the pre-marketing phase. Real-world evidence (RWE), generated from sources such as electronic health records, spontaneous adverse drug reaction reporting systems, insurance claims databases, patient registries, hospital databases, and observational studies, provides valuable information on the long-term safety and effectiveness of medicines in routine clinical practice [6,11].

One of the major advantages of RWE is its ability to identify rare and serious adverse drug reactions that may not be detected during clinical trials because of limited sample sizes and shorter follow-up periods. Continuous post-marketing surveillance enables healthcare professionals and regulatory authorities to detect safety signals at an early stage and take appropriate regulatory action [18]. For example, Rofecoxib was withdrawn after real-world studies demonstrated an increased risk of myocardial infarction and stroke [15,17]. Likewise, Troglitazone was removed from the market after post-marketing reports confirmed cases of severe hepatotoxicity and liver failure [13].

Real-world evidence also provides valuable information on medicine safety in special populations, including pregnant women, children, older adults, and patients with multiple comorbidities who are often underrepresented in clinical trials. A well-known example is Thalidomide, which caused severe congenital abnormalities when used during pregnancy and highlighted the importance of continuous pharmacovigilance [16]. In addition, RWE supports the identification of clinically important drug–drug interactions that occur in routine healthcare settings. For instance, Terfenadine was associated with life-threatening cardiac arrhythmias when administered together with CYP3A4 inhibitors [19].

Furthermore, RWE contributes to continuous benefit–risk assessment throughout the life cycle of a medicine. Regulatory authorities such as the World Health Organization (WHO), the U.S. Food and Drug Administration (FDA), and the European Medicines Agency (EMA) use emerging safety evidence to update prescribing information, introduce risk minimization measures, restrict medicine use, or withdraw medicines when necessary. Integrating

real-world evidence into pharmacovigilance systems strengthens drug safety monitoring, improves patient outcomes, and supports the rational use of medicines [1,3,4,7].

6.1 Regulatory Applications of Real-World Evidence

Real-world evidence has become an essential component of regulatory decision-making worldwide. Regulatory agencies such as the FDA and EMA increasingly use RWE to support post-marketing surveillance, evaluate the benefit–risk profile of medicines, update product labelling, and guide regulatory actions [21,22]. Information obtained from routine clinical practice complements evidence generated through randomized clinical trials by providing data from larger and more diverse patient populations [23,24]. Recent regulatory frameworks also encourage the integration of real-world evidence into pharmacovigilance activities and healthcare policy to improve medicine safety and public health [25,26].

6.2 Artificial Intelligence in Pharmacovigilance

Artificial intelligence (AI) has become an important tool in modern pharmacovigilance by improving the detection of safety signals and enhancing adverse event assessment [27,28]. Machine learning algorithms can analyse large healthcare databases and identify patterns associated with previously unrecognized adverse drug reactions [29,30]. Natural language processing techniques further support pharmacovigilance by extracting useful safety information from electronic health records, clinical notes, scientific literature, and social media platforms [31,32]. As these technologies continue to develop, AI-based pharmacovigilance systems are expected to improve the speed, accuracy, and efficiency of medicine safety monitoring [33].

6.3Patient-Centered Pharmacovigilance

Patient participation has become an important part of modern pharmacovigilance programmes. In recent years, patients have been encouraged to report adverse drug reactions directly, providing valuable information that may not always be captured through reports submitted by healthcare professionals [34,35]. Patient-reported data offer insights into medication adherence, quality of life, treatment outcomes, and the impact of adverse drug reactions on daily living [25,35]. Incorporating patient experiences

into pharmacovigilance activities strengthens patient-centered healthcare and improves the early identification of medicine-related safety concerns [39].

6.4 Digital Health and Sentinel Surveillance Systems

Advances in digital health technologies have significantly improved pharmacovigilance activities. Surveillance programmes such as the Sentinel Initiative use large healthcare databases to continuously monitor the safety of marketed medicines and identify emerging safety concerns [36]. These systems support early signal detection and facilitate timely regulatory action [37]. In addition, electronic health records, wearable devices, and mobile health applications provide real-time clinical information that enhances medicine safety monitoring and strengthens pharmacovigilance practices [38].

6.5 Future Perspectives of Real-World Evidence

The future of pharmacovigilance is expected to rely increasingly on real-world evidence, artificial intelligence, big data analytics, and international collaboration [40,41]. Advanced analytical methods will improve causal inference and strengthen the quality and reliability of evidence generated from routine healthcare data [42,43]. Regulatory agencies across the world are developing new frameworks to expand the use of real-world evidence in medicine safety monitoring and healthcare decision-making [44,45]. International initiatives such as DARWIN EU and other collaborative RWE programmes are expected to improve global pharmacovigilance capabilities and promote better regulatory decision-making [46,47]. Continued developments in artificial intelligence and international safety databases are also likely to enhance signal detection, improve benefit–risk assessment, and support more effective pharmacovigilance systems in the future [48–50].

Overall, the increasing use of real-world evidence, digital technologies, and artificial intelligence is transforming pharmacovigilance by enabling more effective safety monitoring and supporting evidence-based regulatory decision-making.

Discussion

Real-world evidence (RWE) has become an essential component of modern pharmacovigilance by providing valuable information on the safety and

effectiveness of medicines under routine clinical practice. While randomized controlled trials remain the gold standard for evaluating medicines before regulatory approval, they often involve selected patient populations and relatively short follow-up periods. As a result, uncommon, delayed, or long-term adverse drug reactions may not be identified until medicines are used by larger and more diverse populations [3–6].

The availability of real-world data from electronic health records, patient registries, insurance claims databases, spontaneous adverse drug reaction reporting systems, and digital health technologies has significantly strengthened post-marketing surveillance. These data support the early detection of safety signals, assessment of benefit–risk profiles, identification of drug–drug interactions, and evaluation of medicine safety in special populations such as children, older adults, pregnant women, and patients with multiple comorbidities [6,11,18]. Real-world evidence (RWE) has become an essential component of modern pharmacovigilance by providing valuable information on the safety and effectiveness of medicines

under routine clinical practice. While randomized controlled trials remain the gold standard for evaluating medicines before regulatory approval, they often involve selected patient populations and relatively short follow-up periods. As a result, uncommon, delayed, or long-term adverse drug reactions may not be identified until medicines are used by larger and more diverse populations [3–6].

The availability of real-world data from electronic health records, patient registries, insurance claims databases, spontaneous adverse drug reaction reporting systems, and digital health technologies has significantly strengthened post-marketing surveillance. These data support the early detection of safety signals, assessment of benefit–risk profiles, identification of drug–drug interactions, and evaluation of medicine safety in special populations such as children, older adults, pregnant women, and patients with multiple comorbidities [6,11,18]. Several historical examples, including **Thalidomide, Rofecoxib, Troglitazone, Cerivastatin, and Terfenadine**, demonstrate the importance of continuous pharmacovigilance. These medicines

were withdrawn or their use was restricted after real-world evidence revealed serious safety concerns that were not fully recognized during pre-marketing clinical trials [13,15–19]. These cases emphasize the need for continuous monitoring throughout the life cycle of a medicine.

Recent developments in artificial intelligence, machine learning, natural language processing, and digital health technologies have further improved pharmacovigilance by enabling faster signal detection and more efficient analysis of large healthcare datasets [27–33]. In addition, regulatory agencies such as the FDA, EMA, and WHO increasingly recognize the value of real-world evidence in supporting regulatory decisions, updating prescribing information, and strengthening patient safety [21–26].

Despite its advantages, the use of real-world evidence presents several challenges, including incomplete data, reporting bias, variations in data quality, and difficulties in establishing causal relationships as shown in the figure. Addressing these limitations through standardized data collection methods, improved analytical approaches, and international collaboration will enhance the reliability and usefulness of real-world evidence in future pharmacovigilance activities [40–50].

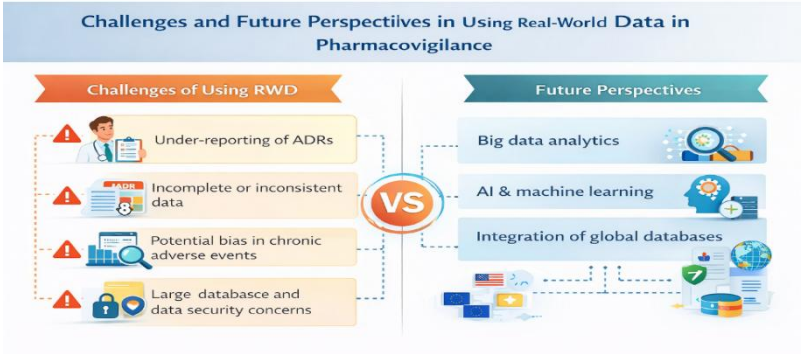

Figure 3. Challenges and Future perspectives of RWE

Conclusion

Real-world evidence (RWE) has become an important component of modern pharmacovigilance by providing valuable information on the safety and effectiveness of medicines in routine clinical practice. It complements evidence obtained from randomized clinical trials by helping to identify rare, delayed, and serious adverse drug reactions that may not be detected before a medicine is approved. Information obtained from electronic health records, patient registries, insurance claims databases, spontaneous adverse drug reaction reporting systems, and digital health technologies has strengthened post-marketing surveillance and improved medicine safety [6,11,12].

The case studies discussed in this review demonstrate how real-world evidence has supported the early identification of important safety concerns and enabled regulatory authorities to take timely action to protect public health [13–20]. In addition, advances in artificial intelligence, machine learning, and digital health technologies are expected to further improve signal detection, benefit–risk assessment, and regulatory decision-making [27–33]. Despite challenges such as incomplete data, reporting bias, and variations in data quality, the growing use of real-world evidence is expected to strengthen pharmacovigilance and support safer use of medicines in diverse patient populations. Continued collaboration among healthcare professionals, researchers, regulatory agencies, and pharmaceutical companies will further improve medicine safety and contribute to better patient care in the future [40–50].

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