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Evolution of Pharmacovigilance: From Spontaneous Reporting to Real-World Evidence

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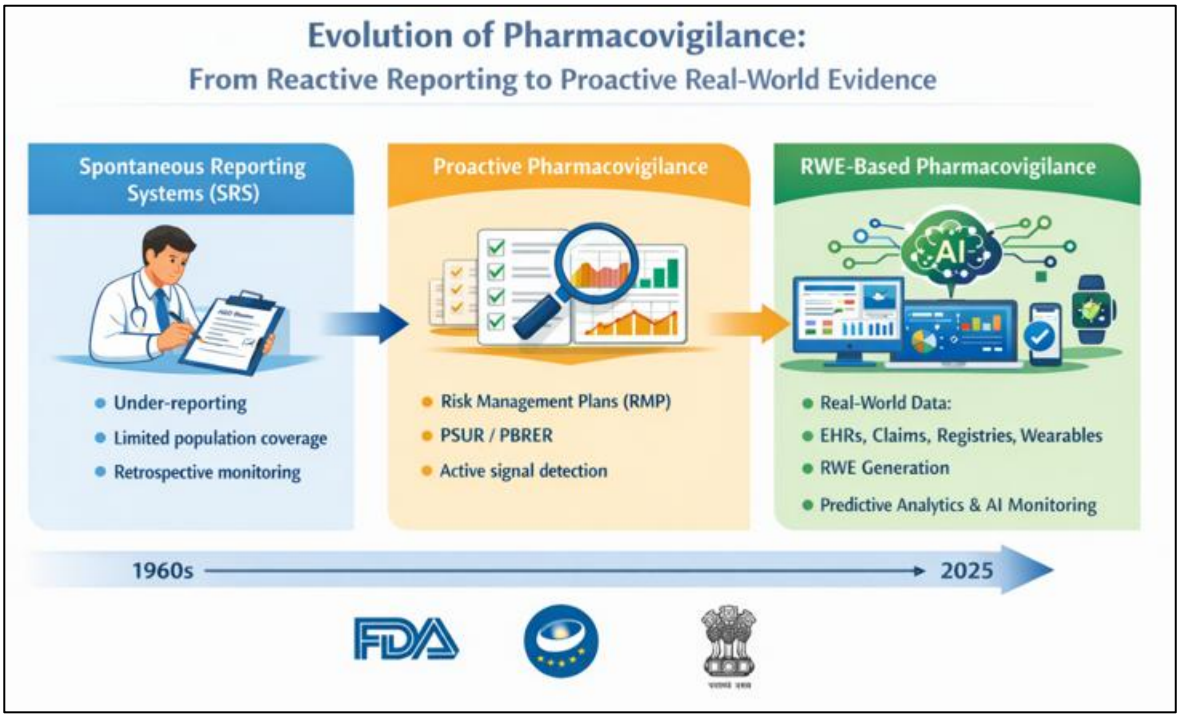
ABSTRACT:

Pharmacovigilance (PV) is a crucial part of safety of the drugs in the product life cycle. The common pharmacovigilance operations had traditionally been based on spontaneous adverse drug reaction (ADR) reporting systems, which, even with their significance, suffered the drawbacks of under-reporting, selection on reporting and slow signal identification. The pharmacovigilance domain has changed over the last 20 years as the combination of proactive risk management, electronic health records, and sophisticated data analytics began to become an integral part of the overall pharmacovigilance concept. Real-world evidence (RWE) has revolutionized the field of pharmacovigilance because it now allows monitoring of the safety of data in real-world (RWD) with the use of registries, claims databases, electronic medical records, and digital health technologies. The incorporation of RWE into regulators frameworks through regulatory decision-making, risk benefit-evaluation, as well as post-marketing surveillance, has progressively gained momentum by regulatory agencies like the US Food and Drug Administration (USFDA), European Medicines Agency (EMA), and Central Drugs Standard Control Organization (CDSCO). This review addresses in detail the history of pharmacovigilance, the shift of the spontaneous reporting systems to the new RWE-based methods, the international regulatory views, the problems, and the future. The changing role of pharmacovigilance in enhancing patient safety, regulatory compliance, as well as, in the overall outcome on the health of the population, is critically evaluated.

Keywords: Pharmacovigilance, Adverse drug reactions, Spontaneous reporting systems, Real-world evidence, Real-world data.

Graphical Abstract-



1. INTRODUCTION-

Pharmacovigilance is an imperative aspect of any health care systems worldwide which is decomposed into the science and actions pertaining to the identification, evaluation, comprehension, and adversity aversion or any other drug-centered issues. The main aim of pharmacovigilance is to protect the health of the population whereby the advantages of medical products have more negative impacts than the gains during the product life cycle. [1] As the drug agents have grown in complexity, so has the pace of drug approval and the utilization of pharmaceuticals in all parts of the world, effective pharmacovigilance frameworks have been set in stone as integral parts of regulatory regimes. [2] In the past, the drug safety assessment was largely limited to preclinical research and the controlled clinical trials. Nevertheless, these trials are inherently predetermined to identify rare, delayed, or population-specific adverse drug reaction (ADRs) because of the small sizes of samples, a few days of the study, and the use of strict inclusion criteria. As a result, a great deal of safety issues are only discovered once a medicinal product is launched into regular clinical use, which is why it is important that there are efficient post-marketing surveillance systems.[3]

Traditional methods of pharmacovigilance were based more on the concept of voluntary reporting or spontaneous reporting systems (SRS), as healthcare professionals (as well as patients more recently) report possible ADRs to national or international regulatory bodies of choice. [4] Although, SRS have been central in the detection of early signs of safety and the inception of disciplinary responding, they are thought to have a number of limitations, such as, under-reporting, biased reporting, inadequate clinical data, and failure to develop rates of occurrence. Such difficulties have induced the regulatory authorities to identify additional and more proactive strategies towards monitoring drug safety. [5]

The recent twenty years has seen a paradigm shift in the field of pharmacovigilance as influenced by the changes in information technology, the growing access to big data in healthcare systems, and new regulatory demands. The real-world data (RWD) integration, encompassing a variety of data sources, including electronic health records, insurance claims databases, patient registries, and digital health technologies has been successful in getting continuous and systematic safety appraisal through real-world evidence (RWE). [6] The promise of RWE is that it will improve signal detection, evaluate the safety outcomes in the long term, and benefit-risk analysis in wider and more diverse populations. The adoption of RWE in pharmacovigilance and regulating personality has become increasingly accepted as regulatory authorities (US Food and Drug Administration, European Medicines Agency and Central Drugs Standard Control Organization) have realized the importance of this method. [7] The shift towards the implementation of risk management strategies, post-authorization safety research and data-driven surveillance programs represents the change of reactive to proactive pharmacovigilance behavior patterns. This development coincides with the efforts of generating better patient safety, surging regulatory performance, and developing evidenced-based public health policies on an international front. [8]

The current review focuses on discussing the transformation of pharmacovigilance systems, between the old system, which is based on spontaneous reporting, and the new one, which necessitates RWE systems. It talks about the historical backgrounds, regulatory views, technological innovations, accompanying issues, and future trends in the field of pharmacovigilance, especially on its increasing importance in the area of regulatory matters.

2. HISTORICAL DEVELOPMENT OF PHARMACOVIGILANCE

Pharmacovigilance is a concept that has gone through a continuous development process due to the increase in awareness of drug-related risks and the requirement to safeguard the health of the citizens. Early drug development and marketing period were very much haphazard in terms of safety considerations and the adverse effects were more likely to be recognized only when used extensively by a large population. There was limited regulatory control and pharmacological surveillance was lacking to a significant degree, and individual clinical observation and anecdotal evidence was used. [9]

2.1 Early Drug Safety Practices

In the pre-20th century, pharmaceutical products used often never underwent rigorous examination on their safety. Regulatory models with a predominantly quality and efficacy approach to control drugs with little systematic safety surveillance. Adverse drug reactions were normally revealed through clinical practice as opposed to formal reporting systems. This informal control resulted in the fact that serious safety concerns were only understood later, which can demonstrate that proper drug safety surveillance systems should be organized.

2.2 Drug Safety Disasters as Catalysts for Change

A number of significant drug-related tragedies acted as milestones in the development of the pharmacovigilance. The thalidomide calamity of the late 1950s and the early 1960s was one of the most important when the utilization of thalidomide during pregnancy caused severe congenital defects in thousands of infants throughout the globe. It was revealed that this tragedy revealed serious loopholes in the drug safety testing and post-marketing supervision and saw the development of more stringent drug approval and monitoring regulatory requirements.

2.3 Emergence of Organized Pharmacovigilance Systems

Due to the increasing attention to safety concerns about drugs in 1960s and 1970s, various countries began formal pharmacovigilance systems. One of the biggest changes was the formation of the World Health Organization (WHO) Programme of International Drug Monitoring in 1968. The objective of this program was to ease international cooperation in the development and measurement of adverse drug reactions through gathering safety information in member countries. [10]

2.4 Regulatory Milestones and Strengthening of Pharmacovigilance

The development of pharmacovigilance was also influenced by the introduction of regulatory milestones, which established the drug safety responsibilities. The reforms in the various regions required post-marketing surveillance, adverse event reporting and periodic safety evaluation. Periodic safety update reporting (PSURs), harmonized as periodic benefit-risk evaluation reports (PBRERs) by the International Council for harmonization (ICH) was a breakthrough in formalized safety evaluation. Pharmacovigilance practices understandably were enhanced further with the development of risk management plans (RMPs) and that of post-authorization safety studies (PASS), which promoted active risk identification and reduction. [11]

2.5 Role of International Harmonization

The international harmonization efforts have been very instrumental in influencing the modern practice of pharmacovigilance. Regulation Agency Standardized definitions, reporting provisions and safety assessment practices across regulatory jurisdictions have been fostered by organizations like the WHO and ICH. The harmonized guidelines have helped in sharing of data across the globe, improving detection of signals, and decision making about regulations. In general, historical evolution of pharmacovigilance is characterized as the ongoing learning experience under the influence of the demands to the health of the population, regulatory changes, and science. The shift to a formal and organized system of pharmacovigilance has provided a foundation to the current practice of modern pharmacovigilance and safety surveillance, including encompassing real-world data and evidence-based safety surveillance.

Table 1. Key Milestones in the Evolution of Pharmacovigilance [12,13]

Period / Year	Milestone	Significance to Pharmacovigilance Development
Early 20th century	Informal drug safety observations	The drug safety was based on clinical experience and anecdotal reporting guidelines.
1937	Sulfanilamide disaster (USA)	Caused the US Federal Food, Drug, and Cosmetic Act (1938), which focused on the safety requirements of drugs.
1950s–1960s	Thalidomide tragedy	This demonstrated the need to strictly monitor drug safety in the post-marketing phase and develop more stringent regulation.
1968	Establishment of WHO Programme for International Drug Monitoring	Introduction of international adverse drug reaction (ADR) monitoring and sharing of information.
1970s	Implementation of national spontaneous reporting systems	Facilitated systematic gathering of ADR reports of medical practitioners.
1990s	Development of pharmacovigilance laws	Increased requirements in ADR reporting and post-marketing surveillance (mandatory).
2000s	The introduction of PSURs and risk management plans (RMPs)	The lifecycle-based safety assessment and proactive risk minimization were encouraged.
2012	Reform of EU pharmacovigilance legislation	Increased patient reporting, improved signal detection with EudraVigilance.
2016 onwards	Introduced real-world data (RWD) and real-world evidence (RWE)	Enabling constantly, high-scale drug safety surveillance based on healthcare databases.
Recent years	Combination of AI, big data, and digital health devices	Advanced signal detection, predictive pharmacovigilance, and regulation decision-making.

3. SPONTANEOUS REPORTING SYSTEMS

Spontaneous reporting systems (SRS) are the foundation of the classical pharmacovigilance and one of the most popular means of post-marketing drug safety monitoring. These are systems in which medical workers, patients, and pharmaceutical firms are ensured to voluntarily submit reports about suspected adverse drug reactions (ADRs). The use of spontaneous reporting has been critical to the early identification of rare, serious, and unexpected adverse effects, which could not be realized in the pre-approval clinical trials. [14]

3.1 Concept and Mechanism of Spontaneous Reporting

The basic principle of spontaneous reporting is the gathering of individual case safety reports (ICSRs) when unfavorable event accompanying a suspected relationship among a medicinal product is detected. Reporting is generally done using standardized forms of reporting, and contains the following information; patient demographics, suspected drug(s), concomitant drugs, description of the adverse event, and clinical outcomes. The regulatory authorities check these reports and input them in the national or international database on safety detection and assessment of signals. Spontaneous reporting systems play the role of hypothesis generation tools, but not confirmationist mechanisms. The safety signal is detected thanks to SRS, and may be investigated with the help of epidemiological studies, clinical trials, or data sources about the real world. In spite of the drawbacks they have, SRS are inseparable because of their simplicity, low prices, and wide areas of use in various healthcare environments. [15]

3.2 Major Global Spontaneous Reporting Systems

As the years passed by, some established spontaneous reporting systems have been either formed or put in place both at national and international levels.

3.2.1 WHO–VigiBase

The world has its largest global database of individual case safety reports in VigiBase, which is conducted by the Uppsala Monitoring Centre (UMC) as part of WHO Programme of International Drug monitoring. It gathers data of ADRs of the member states and assists in the international detection of signals by using advanced statistical techniques.

3.2.2 USFDA MedWatch

MedWatch program is the US Food and Drug Administration adverse event reporting of the drugs, biologics, medical devices and dietary supplements. It enables healthcare professionals and consumers to report suspected ADRs and is the biggest part in post-marketing safety monitoring within the United States.

3.2.3 EMA EudraVigilance

The European Medicines Agency has a central database, EudraVigilance, where the information on suspected ADRs in medicines licensed in the European Economic Area is managed and analysed. It aids in regulation decree-making, identification of signals, and access to security data by the populace.

3.2.4 Pharmacovigilance Programme of India (PvPI)

The national spontaneous reporting system in the Indian market is the Pharmacovigilance Programme of India (PvPI), which is managed by the Indian Pharmacopoeia Commission through the CDSCO. PvPI should strengthen patient safety as its main purpose is to gather, examine, and share information about ADRs on a national level. [16]

3.3 Role of Healthcare Professionals and Patients

The usual producers of spontaneous reporting systems have been healthcare professionals such as physicians, pharmacists and nurses. Their clinical competence will facilitate proper diagnosis and reporting of possible ADRs. Patient reporting has become recognized in recent years as a valuable source of information on drug safety as regarded by the patient to quality-of-life issues and long-term adverse effects. Regulatory bodies have been very supportive to facilitate patient engagement in pharmacovigilance in an attempt to increase reporting rates and desirability of safety data. The healthcare professional report as well as the patient report has enhanced the entire efficiency of the spontaneous reporting systems. [17]

3.4 Regulatory Importance of Spontaneous Reporting Systems

Regulatory-wise, the issue of post-marketing safety responsibilities is necessitated by the necessity of the presence of the so-called spontaneous reporting systems. Data obtained by SRS are used to add to signal detection, risk assessment, labeling updates, safety communications and regulation (restrictions, withdrawals or minimum risks). In spite of the development of high-level pharmacovigilance methodologies, SRS still remain an important aspect of international drug safety monitoring systems. [18]

Table 2. Strengths and Limitations of Spontaneous Reporting Systems (SRS) [19]

Aspect	Strengths	Limitations
Signal detection	Effective for identifying rare, serious, and unexpected adverse drug reactions	Unable to establish incidence or prevalence rates
Scope of coverage	Covers a wide range of drugs and patient populations	Subject to under-reporting and selective reporting
Cost and feasibility	Relatively low-cost and easy to implement	Data quality often depends on reporter motivation and expertise
Speed of reporting	Allows early detection of safety signals post-marketing	Delays in reporting may hinder timely signal assessment
Data source	Accepts reports from healthcare professionals and patients	Reports often contain incomplete or missing clinical information
Regulatory utility	Supports regulatory actions such as label changes and risk communication	Cannot confirm causality without further investigation
Global applicability	Widely adopted and harmonized across countries	Variability in reporting practices among regions

4. TRANSITION FROM REACTIVE TO PROACTIVE PHARMACOVIGILANCE

The early pharmacovigilance systems were mostly reactive in the sense that they were aimed at identifying and evaluating the adverse drug reactions upon their development and subsequent reporting under the spontaneous reporting systems. Although this method has played a great role in identification of early safety signals, its use was intertwined with voluntary reporting and retrospective analysis thereby undermining its capability of preventing or predicting drug-related risks. The pressures of growing regulatory demands alongside the growing complexity of drugs and their international exposure were compelling change towards a more proactive approach of pharmacovigilance. [20]

4.1 Limitations of Reactive Pharmacovigilance

Reactive pharmacovigilance mainly relies on passive gathering of the adverse events reports which frequently leads to late signal identification and inadequate safety evaluation. The Company has problems with under-reporting, exposure and reporting bias which impede timely reporting in case of emerging risks. Besides, reactive systems are not as effective in long-term negative effect, drug-drug interaction and safety problems in special population like pediatrics, geriatrics and comorbid patients. These constraints made it apparent that the systematic risk detection and management methods should go beyond the post-hoc knowledge of reported bad events. 4.2 Risk Management and Lifecycle- Based Approaches Introduction. [21]

4.2 Introduction of Risk Management and Lifecycle-Based Approaches

In response to this lack of reliability in reactive systems, regulatory agencies put forward formal risk management systems that focus on a sustained safety supervision on the lifecycle of the drug. Risk management plans (RMPs) were formulated to determine the probable and the known risk, take a description of the pharmacovigilance activities, and deliberate the risk reduction plans. Implementing RMPs was an important step in achieving the goal of proactive pharmacovigilance since it obliges sponsors to foresee and restrict safety issues prior to extensive clinical usage. Equally, with periodic safety update reports (PSURs) later harmonized as periodic benefit-risk evaluation report (PBRERs), regular cumulative assessment of cumulative safety data became possible. These reports offered an inclusive perspective on the changing benefit-risk profile of medicinal products, which assist in benefiting the right time to take regulatory decisions. [22]

4.3 Enhanced Signal Detection and Safety Monitoring

Greater investments in data management and technologies of statistical processes led to proactive signal detection strategies. Regulatory bodies started to use quantitative signal recognition methods, data mining models, and centralized databases on safety to detect trends that may represent the emergence of risks. These aids facilitated the previous examination of safety indications and enhanced hierarchy of regulatory events. Proactive pharmacovigilance was further enhanced in the integration of post-authorization safety studies (PASS): now targeted research of particular safety concerns could be conducted under real-world conditions. PASS also developed strong evidence to prove or disapprove safety signals as observed by spontaneous reporting systems. [23]

4.4 Regulatory Drivers of Proactive Pharmacovigilance

The global regulatory reforms have also been useful in facilitating proactive pharmacovigilance. The pharmacovigilance law in the European Union focused on the benefits of continuous benefit risk evaluation, transparency and patient involvement. In the same vein, USFDA also established programs like Sentinel System to aid on active oversight of products in the market. The consternation of Pharmacovigilance Programme of India (PvPI) in India is an indicator of increased attention to systematic safety monitoring and focus on regulations. Together, these regulatory efforts highlight a paradigm shift in the concept of pharmacovigilance between reactive and proactive, as the foundation on which real-world data and real-world evidence are being integrated into the current systems of drug safety surveillance. [24]

5. REAL-WORLD DATA (RWD) IN PHARMACOVIGILANCE

Real-world data (RWD) are data that can be faced with the health status of patients and the output of healthcare that are gathered on routine basis other than conventional randomized clinical trials. RWD have become a key needful supplement in pharmacovigilance systems because they facilitate active and ongoing monitoring of drug safety in practical clinical environments as a complement to spontaneous reporting systems. The growing digitization of the healthcare systems has greatly increased the accessibility and applicability of the RWD to the regulatory and safety assessment purposes. [25]

5.1 Sources of Real-World Data

RWD employed in pharmacovigilance is obtained based on various sources of healthcare and non-healthcare. The main sources are electronic health records (EHRs), insurance claims and reimbursement databases, patient registries, hospital information systems and prescription databases. These resources are longitudinal databases of drug exposure, clinical outcomes, comorbidities, and healthcare usage in varied patients. Other sources of RWD, including digital health platforms, wearable devices, mobile health applications, as well as patient-reported outcomes, have since become part of the RWD landscape in the past few years. These measures of data provide real-time data related to adherence to treatment, lifestyle factors, and long-term safety status, which is underrepresented in conventional pharmacovigilance systems. [26]

5.2 Role of RWD in Enhancing Pharmacovigilance

The introduction of the concept of RWD in the pharmacovigilance field enables a better safety monitoring system since a number of shortcomings that spontaneous reporting systems have are eliminated. In contrast to SRS, RWD include denomicator data and allow the incidence rates to be estimated and comparative safety studies to be performed. They can also be used to assess drug safety in special groups of patients, including the elderly population, pregnant women, and people with several comorbid conditions. RWD accommodates active surveillance models, which allows screening big housing data routinely and obtaining indicators of possible hazards. This active practice improves the promptness and strength of signal detection and presence of the regulatory authorities to observe drug safety through the product lifecycle. [27]

5.3 Regulatory Relevance of RWD

The regulatory agencies have been driving towards making greater use of RWD in the pharmacovigilance. Both frameworks prepared by the agencies, i.e. USFDA, EMA and CDSCO, lay significant emphasis over the application of RWD to substantiate post-marketing safety promises, post-authorization safety trials, and benefit-risk analyses. Although the idea of the RWD might not prove causality itself, it gives crucial contextual and supporting evidence by which regulatory choices and risk management action plans should be made. [28]

6. REAL-WORLD EVIDENCE (RWE): APPLICATIONS IN DRUG SAFETY

Real-world evidence (RWE) is that clinical evidence of either usage, benefit, or risk of a medical product based on the analysis of real-world data. RWE is the analytical and interpretive result of RWD in pharmacovigilance and increasingly important in evaluating drug safety, regulating drug safety and protecting the health of the population in general. [29]

6.1 Generation of Real-World Evidence

RWE is created as a result of applying epidemiological techniques, statistical methods, and data analytics to RWD sources. The typical forms of study designs are that of observational cohort studies, case-control studies, pragmatic trials, and database studies. These techniques enable investigators and regulators evaluate associations amid drug exposure and undesirable results in normal clinical practice settings. The capacity to derive meaningful evidence out of huge and complicated data has been augmented through the improvement of data science, machine learning, and artificial intelligence. These can be used to facilitate automated signal recognition, pattern recognition and risk stratification, which enhance the exemplar worth of RWE in drug vigilance. [30]

6.2 Applications of RWE in Drug Safety Monitoring

RWE can be utilized in a variety of activities in the spectrum of pharmacovigilance. It becomes especially useful when either validating or disqualifying safety signals reported as such by means of spontaneous reporting systems. RWE allows the evaluation of the safety of a large number of patients over a long period of time, unusual adverse event causes, and delayed outcomes that are hard to detect in pre-approval clinical trials. RWE also facilitates comparative safety appraisal among therapeutic alternatives as well as aids the evaluation of drug-drug interactions and safety in the real-life clinical settings. It also gives vital information on drug use habits, compliance, and off-label use, which could affect the general safety profile of medicinal products. [31]

6.3 Regulatory Use of RWE in Pharmacovigilance

RWE is increasingly become the foundation of regulatory actions by regulatory authorities to shape post-marketing regulatory decisions, such as labeling changes, reduction of risks, and restrictions of usage. RWE is fueled to be used in post-authorization safety studies (PASS) and as supplementary evidence in periodic benefit-risk assessment reports. This has very much been in cases where quick safety evaluation is needed especially in case of emergency in the health of the population or regulatory quick-track. On a noted despite its increasing significance, there is a need to pay a lot of attention to the data quality, study design, and methodological rigor when regulatory acceptance of RWE is concerned. This has led to the regulatory agencies publishing guidance documents that specify the best practices in the generation and use of RWE to pharmacovigilance. [32]

Table 3. Comparison of Spontaneous Reporting Systems (SRS) and RWE-Based Pharmacovigilance. [33,34]

Aspect	Spontaneous Reporting Systems (SRS)	Pharmacovigilance based on RWE.
Data Source	Voluntary reports from healthcare professionals and patients	Real-world data from EHRs, claims databases, registries, wearables, and digital health platforms
Nature of Data	Individual case safety reports (ICSRs), often qualitative	Large-scale, structured or unstructured datasets enabling quantitative analysis
Coverage	Limited by voluntary reporting and under-reporting	Broad coverage of diverse patient populations, including special populations
Signal Detection	Hypothesis-generating; identifies rare and serious ADRs	Proactive and hypothesis-testing; identifies patterns, trends, and long-term safety issues
Timeliness	Often delayed due to voluntary submission	Near real-time or continuous monitoring depending on data source and infrastructure
Causality Assessment	Limited; cannot establish incidence or prevalence	Provides contextual and comparative insights; supports risk–benefit evaluation but still requires careful interpretation
Regulatory Utility	Supports label updates, safety communications, and regulatory actions	Supports post-authorization safety studies, risk management plans, and evidence-based regulatory decision-making
Strengths	Low-cost, simple, widely implemented globally	Large-scale, representative, enables active surveillance, evaluates long-term outcomes
Limitations	Under-reporting, incomplete information, reporting bias	Data quality, heterogeneity, privacy concerns, methodological complexity

7. REGULATORY PERSPECTIVES – USFDA, EMA, CDSCO

Regulatory authorities in various countries have been playing a key role in the evolution of pharmacovigilance, with each of them having an entablature of assuring drug safety, protect the health of the population, as well as standardize post-marketing surveillance activities. The contemporary pharmacovigilance practices are indicative of the regulatory transformation toward the data-driven and reactive approach to safety. [35]

7.1 United States Food and Drug Administration (USFDA)

USFDA is bearing a central role in drug safety in the post-marketing phase by several initiatives like MedWatch Program: It enables medical practitioners and patients to report adverse drug reactions, product quality, and medication errors. Sentinel System: It was launched in 2008; the system is a national active surveillance initiative which uses electronic healthcare information through numerous sources which is used to examine the safety of promoted drugs in close real-time. RWE utilization: The USFDA has issued guidance to promote real-world evidence utilization in support regulatory tasks, such as label alterations, post-marketing safety examination, and expedited approach of approval. [36]

7.2 European Medicines Agency (EMA)

EMA leads the pharma vigilance in the European Economic Area (EEA) by EudraVigilance: An integrated hubs health data, where it is possible to manage and analyze suspected adverse reactions to be used to provide early warnings on the signal and also on risk assessment. Post-Authorization Safety Studies (PASS) and Risk Management Plans (RMPs): make sure that safety risks are actively countervailed. Regulatory Reforms: This was complemented by the 2012 legislation on pharmacovigilance in the EU that increased transparency and patient involvement and optimized on the employed signal detection methodologies, further driving the proactive approach to drug safety. [37]

7.3 Central Drugs Standard Control Organization (CDSCO), India

The national pharmacovigilance system of India is managed by the CDSCO on the Pharmacovigilance Programme of India (PvPI) like PvPI Network: Includes, summarizes, and evaluates adverse drug reaction in healthcare facilities in the country. Awareness and Training: Services a guidance and training to medical workers on ADR reporting and pharmacovigilance practices. Conformity to Global Standards: Consonant with WHO pharmacovigilance principles, and with ICH principles, business people can promote harmonization with international regulatory procedures. [38]

7.4 Global Harmonization and Trends

The international organizations, like the international council on harmonization (ICH) and WHO guidelines, strive to standardize the definitions, reporting needs, and safety assessment techniques. Harmonization facilitates international co-operation, exchange of data and ensuring uniformity of decisions on regulatory decisions, which indicates the increased convergent trend of pharmacovigilance practices globally. [39]

8. CHALLENGES AND LIMITATIONS OF RWE-BASED PHARMACOVIGILANCE

Although pharmacovigilance using real-world evidence (RWE) has the potential to be transformative, its application is associated with multiple methodological, operational, and regulatory challenges that should be overcome to achieve reliability and regulatory acceptance.

8.1 Data Quality and Standardization

RWE is based on different sources of heterogeneous real-world data (RWD), such as electronic health records, claims database, patient registry, and wearable devices. The validity of analyses can be affected by variability in the format of the data, coding scheme, completeness and accuracy. The absence of standardized data collection and reporting inconsistency of clinical outcomes makes cross dataset and region comparability difficult.

8.2 Privacy and Ethical Concerns

Ethical and privacy issues are of great concern to the use of patient-level RWD. Data protection rules including HIPAA in the US and GDPR in Europe and other privacy laws in the region should be adhered to. Anonymity of patients, storage of data, and access control make RWE-based pharmacovigilance more complex.

8.3 Methodological Challenges

Observational data are not randomized, and this creates the problem of confounding and bias. Causation between exposure to drugs and undesirable outcomes cannot be determined easily and thus advanced statistical methods, including propensity score matching, inverse probability weighting, and sensitivity analysis, are needed. Interpretability can also be curtailed by the misclassification of exposures or outcomes.

8.4 Integration with Traditional Pharmacovigilance

RWE is not a substitute of classic spontaneous reporting system (SRS). The adoption of the RWE findings into the current pharmacovigilance processes is an issue that needs a regulatory body, standardized protocols, and interdisciplinary expertise that the organization might lack.

8.5 Regulatory and Implementation Challenges

As much as regulatory bodies are now willing to accept RWE, there are no final decisions regarding acceptance. Among the problems, there are the definition of suitable study designs, endpoints, and methods of analysis. Regulatory differences in jurisdictions could adversely affect or slow the international application of RWE results in safety assessment. [5,29]

9. FUTURE PERSPECTIVES AND EMERGING TRENDS

The future of drug surveillance is interventions based on the combination of innovative technologies and real-life data on interventions and predictive analytics to generate preventive and patient-centered safety surveillance systems.

9.1 Predictive Pharmacovigilance

The forecast of the possible negative event prior to its occurrence is anticipated to be possible through artificial intelligence (AI) and machine learning (ML) models by utilizing previous ADR data and patient-specific risk factors. Personalized risk mitigation plans and predictive models can be used to assist in precision pharmacovigilance.

9.2 Digital Health and Patient-Centered Monitoring

Mobile health application, wearables, and telemedicine platforms will become the source of patient-generated health data that allows constant real-time tracking of safety and more precise insights into the effects of drugs in everyday life.

9.3 Global Harmonization and Regulatory Convergence

The harmonization of standards related to pharmacovigilance supported by ICH, WHO and collaboration with regulatory bodies will guarantee the facilitation of the transfer of data across the borders, standardized evaluation of signals and the prompt regulatory action grounded on RWE.

9.4 Integration of Multi-Modal Data

The overlap between genomics, metabolomics, digital health data, and social media analytics and traditional RWD will benefit the profiling of safety in their totality and early-on adverse occurrences.

9.5 Real-Time Decision Support Systems

Dashboards with automated mechanisms and decision support systems powered by AI will enable regulators and pharmaceutical companies to track safety trends on a timely basis and take measures to reduce risks in a short period of time. [40,41]

10. CONCLUSION

Pharmacovigilance is turning into a more interactive, data- Based, proactive, and technology-enabled science instead of a more reactive and spontaneous reporting-based system. The fact that real-world data and real-world evidence have broadened the spectrum of drug safety monitoring is that they permit maintaining continuous, large-scale, patient-centred assessment of medicine products. These developments have been adopted by regulatory authorities such as the USFDA, EMA and CDSCO using well-developed frameworks, post-authorization safety, and risk management plans. It is undeniable that, regardless of related data quality and methodological constraints, privacy, and regulatory harmonization, RWE, advanced analytics, and digital health technology integration are the hallmarks of a new dawn in pharmacovigilance. The recently developed trends, including predictive pharmacovigilance, real-time intelligence, and multi-modal data integration, can all contribute to patient safety, optimized regulatory decision-making, and more efficient risk, benefit assessment. The current transformation in pharmacovigilance highlights the importance of the field in protecting the health of the populace, informing evidence-based regulatory actions and facilitating the creation of improved and safer therapeutic interventions. The further cooperation of regulators, healthcare providers, patients and industry, and the usage of the innovative technologies will conceptualize the future of the pharmacovigilance practices in the world.

11. REFERENCES

1. *Pharmacovigilance*. (2025, December 12). https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance
2. Hammad, T. A., Afsar, S., Le-Louet, H., & Kugener, V. F. (2023). Navigating a transforming landscape: the evolving role of pharmacovigilance physicians in drug development and implications for future challenges and training requirements. *Frontiers in Drug Safety and Regulation*, *3*, 1257732. https://doi.org/10.3389/fdsfr.2023.1257732
3. Loke, Y. K., & Derry, S. (2001). Reporting of adverse drug reactions in randomised controlled trials – a systematic survey. *BMC Clinical Pharmacology*, *1*(1), 3. https://doi.org/10.1186/1472-6904-1-3
4. Desai, M. (2022). Pharmacovigilance and spontaneous adverse drug reaction reporting. *Perspectives in Clinical Research*, *13*(4), 177–179. https://doi.org/10.4103/picr.picr_169_22
5. Crisafulli, S., Bate, A., Brown, J. S., Candore, G., Chandler, R. E., Hammad, T. A., Lane, S., Maro, J. C., Norén, G. N., Pariente, A., Russom, M., Salas, M., Segec, A., Shakir, S., Spini, A., Toh, S., Tuccori, M., Van Puijenbroek, E., Trifirò, G., & Pharmacovigilance, T. R. E. a. B. D. S. I. G. O. T. I. S. O. (2025). Interplay of Spontaneous Reporting and Longitudinal Healthcare Databases for Signal Management: Position Statement from the Real-World Evidence and Big Data Special Interest Group of the International Society of Pharmacovigilance. *Drug Safety*, *48*(9), 959–976. https://doi.org/10.1007/s40264-025-01548-3
6. Yang, J., & Li, F. (2025). The impact of technological progress on pharmacovigilance. In Pharmaceutical science. https://doi.org/10.5772/intechopen.1006906
7. Tripathi, A., Kumar, A., & Das, D. (2026). Real-World Evidence and signal Detection: Emerging methodologies in Indian Pharmacovigilance practice. JOURNAL OF ADVANCE AND FUTURE RESEARCH, 4(1). https://doi.org/10.56975/jaafr.v4i1.502435
8. Menang, O., Kuemmerle, A., Maigetter, K., & Burri, C. (2023). Strategies and interventions to strengthen pharmacovigilance systems in low-income and middle-income countries: a scoping review. BMJ Open, 13(9), e071079. https://doi.org/10.1136/bmjopen-2022-071079
9. Fornasier, G., Francescon, S., Leone, R., & Baldo, P. (2018). An historical overview over Pharmacovigilance. *International Journal of Clinical Pharmacy*, *40*(4), 744–747. https://doi.org/10.1007/s11096-018-0657-1
10. Monni, S. (2025, February 21). *History of pharmacovigilance: evolution and progress in drug safety surveillance*. SafetyDrugs. https://safetydrugs.it/en/history-of-pharmacovigilance/
11. Shaikh, S. S., Bharati, A., Dubey, T., Thakur, R., Bhosale, K., & Bhoir, P. (2024). A Review article of pharmacovigilance and studies of clinical research for health care. *IP International Journal of Comprehensive and Advanced Pharmacology*, *9*(2), 116–124. https://doi.org/10.18231/j.ijcaap.2024.017
12. Khan, M. a. A., Sara, T., & Babar, Z. (2024). Pharmacovigilance: the evolution of drug safety monitoring. *Journal of Pharmaceutical Policy and Practice*, *17*(1), 2417399. https://doi.org/10.1080/20523211.2024.2417399
13. Ashwlayan, V. D., & Nimesh, S. (2018). Pharmacovigilance: an Overview. *International Journal of Pharmacovigilance*, *3*(1), 1–6. https://doi.org/10.15226/2476-2431/3/1/00124
14. Lindquist, M. (2008). VigiBase, the WHO Global ICSR Database System: Basic facts. *Drug Information Journal*, *42*(5), 409–419. https://doi.org/10.1177/009286150804200501
15. Negru, P. A., Tit, D. M., Radu, A. F., Bungau, G., Corb Aron, R. A., & Marin, R. C. (2025). Comparative pharmacovigilance analysis of approved and repurposed antivirals for COVID-19: Insights from EudraVigilance data. *Biomedicines*, *13*(6), 1387. https://doi.org/10.3390/biomedicines13061387
16. Kalaiselvan, V., Thota, P., & Singh, G. N. (2014). Pharmacovigilance Programme of India: Recent developments and future perspectives. *Drug Safety*, *37*(9), 703–710. https://doi.org/10.1007/s40264-014-0202-7
17. Hazell, L., & Shakir, S. A. W. (2006). Under-reporting of adverse drug reactions: A systematic review. *Drug Safety*, *29*(5), 385–396. https://doi.org/10.2165/00002018-200629050-00003
18. Kessler, D. A. (1993). Introducing MEDWatch: A new approach to reporting medication and device adverse effects and product problems. *JAMA*, *269*(21), 2765–2768. https://doi.org/10.1001/jama.1993.03500210045030
19. Olsson, S., Pal, S. N., Stergachis, A., & Couper, M. (2010). Pharmacovigilance activities in 55 low- and middle-income countries: A questionnaire-based analysis. *Drug Safety*, *33*(8), 689–703. https://doi.org/10.2165/00002018-201033080-00007
20. Ball, R., Robb, M., Anderson, S. A., & Dal Pan, G. J. (2016). The FDA's Sentinel Initiative: A comprehensive approach to medical product surveillance. *Clinical Pharmacology & Therapeutics*, *99*(3), 265–268. https://doi.org/10.1002/cpt.320
21. Hazell, L., & Shakir, S. A. W. (2006). Under-reporting of adverse drug reactions: A systematic review. *Drug Safety*, *29*(5), 385–396. https://doi.org/10.2165/00002018-200629050-00003
22. Butler, D., Ding, J., & Dodd, C. (2021). Regulatory experience of handling Risk Management Plans (RMPs) for medicinal products in the EU. *Expert Opinion on Drug Safety*, *20*(7), 815–826. https://doi.org/10.1080/14740338.2021.1909569
23. Fukazawa, C., Kubota, K., & Kimura, T. (2018). Significance of data mining in routine signal detection: Analysis based on the safety signals identified by the FDA. *Pharmacoepidemiology and Drug Safety*, *27*(12), 1402–1408. https://doi.org/10.1002/pds.4672
24. Almas, M. F., Girardi, A., Crisafulli, S., Gvozdanovic, K., Hakkarainen, K. M., Hyeraci, G., Hoogendoorn, W. E., Rillmann, B., Roberto, G., & Vitturi, G. (2025). Identifying regulatory outcomes of non-interventional post-authorisation safety studies (PASS) in

the European repository of studies using publicly available information. *Frontiers in Drug Safety and Regulation*, *5*, 1574430. https://doi.org/10.3389/fdsfr.2025.1574430

25. Coloma, P. M., Schuemie, M. J., Herings, R., Gini, R., Mazzaglia, G., Picelli, G., Fornari, C., Pedersen, L., van der Lei, J., Sturkenboom, M., & Trifirò, G. (2015). Using real-world healthcare data for pharmacovigilance signal detection—The experience of the EU-ADR project. *Expert Review of Clinical Pharmacology, 8*(1), 95–102. https://doi.org/10.1586/17512433.2015.992878
26. Dimitsaki, S., Natsiavas, P., & Jaulent, M.-C. (2024). Applying AI to structured real-world data for pharmacovigilance: Scoping review. *Journal of Medical Internet Research, 26*, e57824. https://doi.org/10.2196/57824
27. Coloma, P. M., Trifirò, G., Patadia, V., & Sturkenboom, M. (2013). Postmarketing safety surveillance: Where does signal detection using electronic healthcare records fit into the big picture? *Drug Safety, 36*(3), 183–197. https://doi.org/10.1007/s40264-013-0090-1
28. Desai, R. J., Matheny, M. E., Johnson, K., Marsolo, K., Curtis, L. H., Nelson, J. C., Brown, J. S., Toh, S., Reich, C. G., Surfeit, R., Wang, M., Weiskopf, N., Baker, M. A., & Frank, S. A. (2021). Broadening the reach of the FDA Sentinel system: A roadmap for integrating electronic health record data in a causal analysis framework. *NPJ Digital Medicine, 4*(1), 170. https://doi.org/10.1038/s41746-021-00522-8
29. Dang, A. (2023). Real-world evidence: A primer. *Pharmaceutical Medicine, 37*(1), 25–36. https://doi.org/10.1007/s40290-022-00456-6
30. Chen, J., Zhan, X., & Wang, Y. (2024). Data science methods for real-world evidence generation: Study design, analytics, and applications. *Therapeutic Innovation & Regulatory Science, 58*(4), 753–765. https://doi.org/10.1007/s43441-024-00570-6
31. Gauffin, O., Brand, J. S., Vidlin, S. H., Kurz, X., & Cave, A. (2023). Supporting pharmacovigilance signal validation and prioritization with analyses of routinely collected health data: Lessons learned from an EHDEN network study. *Drug Safety, 46*(12), 1335–1352. https://doi.org/10.1007/s40264-023-01353-w
32. Cave, A., Kurz, X., & Arlett, P. (2019). Real-world data for regulatory decision making: Challenges and possible solutions for Europe. *Clinical Pharmacology & Therapeutics, 106*(1), 36–39. https://doi.org/10.1002/cpt.1426
33. Crisafulli, S., Bate, A., Brown, J. S., Candore, G., Chandler, R. E., Hammad, T. A., Lane, S., Maro, J., Norén, G. N., Pariente, A., Russom, M., Salas, M., Segec, A., Shakir, S., Spini, A., Toh, S., Tuccori, M., van Puijenbroek, E., & Trifirò, G. (2025). Interplay of spontaneous reporting and longitudinal healthcare databases for signal management: Position statement from the Real-World Evidence and Big Data Special Interest Group of the International Society of Pharmacovigilance. *Drug Safety, 48*(9), 959–976. https://doi.org/10.1007/s40264-025-01548-3
34. Pacurariu, A. C., Straus, S. M., Trifirò, G., Schuemie, M. J., Gini, R., Herings, R., Mazzaglia, G., Picelli, G., Scotti, L., Pedersen, L., Arlett, P., van der Lei, J., Sturkenboom, M. C., & Coloma, P. M. (2015). Useful interplay between spontaneous ADR reports and electronic healthcare records in signal detection. *Drug Safety, 38*(12), 1201–1210. https://doi.org/10.1007/s40264-015-0341-5
35. Khan, M. A. A., Hamid, S., & Babar, Z.-U.-D. (2022). Pharmacovigilance practices in South Asian Association for Regional Cooperation countries: The need for collaboration. *Journal of Pharmaceutical Health Services Research, 12*, 789103. https://doi.org/10.1093/jphsr/rmac046
36. Ball, R., Robb, M., Anderson, S. A., & Dal Pan, G. J. (2016). The FDA's Sentinel Initiative: A comprehensive approach to medical product surveillance. *Clinical Pharmacology & Therapeutics, 99*(3), 265–268. https://doi.org/10.1002/cpt.320
37. Bahri, P., Genov, G., Arlett, P., Šariņi, V. M., Korakianiti, E., Nolte, A., Huber, M., & Straus, S. M. J. M. (2024). The STAR Compass to guide future pharmacovigilance based on a 10-year review of the strengthened EU system. *Drug Safety, 47*(10), 941–956. https://doi.org/10.1007/s40264-024-01451-3
38. Kalaiselvan, V., Thota, P., & Singh, G. N. (2016). Pharmacovigilance Programme of India: Recent developments and future perspectives. *Indian Journal of Pharmacology, 48*(6), 624–628. https://doi.org/10.4103/0253-7613.194855
39. Lavenburg, D., Gumpina, R., & Cope, J. (2018). Global pharmacovigilance regulations: Call for re-harmonization. *Therapeutic Innovation & Regulatory Science, 52*(6), 721–727. https://doi.org/10.1177/2168479018801592
40. Bate, A., Čović, D., & Dodd, C. (2022). Analytical/pharmacovigilance methods to support the development of predictive/precision medicine A meeting report. *Drug Safety, 45*(6), 577–585. https://doi.org/10.1007/s40264-022-01155-0
41. Kilic, B., Welsink-Karssies, P. J., Straus, S. M. J. M., & van der Schyf, C. (2024). Patient-generated health data in pharmacovigilance: A systematic review to inform regulatory frameworks. *Drug Safety, 47*(1), 1–13. https://doi.org/10.1007/s40264-023-01408-y

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