Current Regulatory Landscape Reviews Evolving Pharmacovigilance Systems, Comparative Frameworks, and the Role of Real-World Evidence in India

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Abstract— **Objective: Pharmacovigilance (PV) plays a vital role in ensuring drug safety by maintaining a favorable benefit risk balance throughout a product's lifecycle. In India, the Pharmacovigilance Programme of India (PvPI) has strengthened drug safety monitoring, but challenges such as underreporting, data quality, and limited integration with real-world evidence (RWE) persist. Comparative insights with global systems such as the European Medicines Agency (EMA) highlight both progress and gaps in India's evolving framework. This review aims to critically assess India's pharmacovigilance system, compare regulatory practices between the Central Drugs Standard Control Organization (CDSCO) and EMA, and evaluate the role of RWE in enhancing post-marketing surveillance (PMS)**

Methodology: A systematic review was conducted following PRISMA 2020 guidelines. All eligible sources comprising peer-reviewed research, regulatory guidelines, and policy documents were analyzed through narrative synthesis and comparative tabulation.

Results: Findings reveal that PvPI has expanded to over 500 ADR monitoring centers, significantly contributing to global safety databases. However, ADR underreporting, infrastructural disparities, and weak patient participation remain challenges. The CDSCO framework demonstrates notable alignment with EMA principles but lacks comprehensive enforcement of risk management plans, OTC oversight, and electronic interoperability. RWE integration in India remains nascent, though initiatives such as the Ayushman Bharat Digital Mission (ABDM) provide opportunities for data-driven regulatory decisions.

Conclusion: India's pharmacovigilance system is at a transformative stage. Strengthening regulatory enforcement, harmonizing with EMA practices, and systematically integrating RWE and digital health platforms can elevate India's PV framework into a proactive, technology-enabled, and globally harmonized model for patient safety

Index Terms— **Pharmacovigilance Programme of India (PvPI), Central Drugs Standard Control Organization (CDSCO), European Medicines Agency (EMA), Adverse Drug Reactions (ADRs), Real-World Evidence (RWE), Post-Marketing Surveillance (PMS), Regulatory Harmonisation, Digital Health, Drug Safety**

List of Abbreviations
ABDM – Ayushman Bharat Digital Mission
ADR – Adverse Drug Reaction
AI – Artificial Intelligence
AMC – Adverse Drug Reaction Monitoring Centre
CDSCO – Central Drugs Standard Control Organisation
DB – Database
DPDP – Digital Personal Data Protection
EC – European Commission
EHR – Electronic Health Record
EMA – European Medicines Agency
EU – European Union
FDA – Food and Drug Administration (United States)
GVP – Good Pharmacovigilance Practices
HCP – Healthcare Professional
ICH – International Council for Harmonisation
ICSR – Individual Case Safety Report
IPC – Indian Pharmacopoeia Commission
MAH – Marketing Authorization Holder
MedDRA – Medical Dictionary for Regulatory Activities
NCC – National Coordinating Centre
NHA – National Health Authority
NLP – Natural Language Processing
NPP – National Pharmacovigilance Programme
OTC – Over-the-Counter
PASS – Post-Authorization Safety Study
PM-JAY – Pradhan Mantri Jan Arogya Yojana
PMS – Post-Marketing Surveillance

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSUR – Periodic Safety Update Report
PV – Pharmacovigilance
PvPI – Pharmacovigilance Programme of India
QPPV – Qualified Person Responsible for Pharmacovigilance
RMP – Risk Management Plan
RWD – Real-World Data
RWE – Real-World Evidence
UMC – Uppsala Monitoring Centre
US FDA – United States Food and Drug Administration
WHO – World Health Organization
WHO-ART – World Health Organization Adverse Reaction Terminology

I. INTRODUCTION

Pharmacovigilance (PV) is defined by the World Health Organization (WHO) as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine-related problem" [1]. It is an essential part of the modern healthcare system, which ensures that drugs available in the market maintain a favorable benefit–risk profile throughout their lifecycle [2]. The global emphasis on PV has intensified over recent decades due to rapid advancements in pharmaceutical innovation, increasing complexity of therapeutic modalities, and heightened patient safety expectations [3].

In India, the need for robust PV practices is particularly pronounced. The country is one of the largest global manufacturers of pharmaceuticals, ranking third in volume and fourteenth in value [4]. The vast domestic market with extensive export of medicines, makes India a crucial player in the global market. Also, India serves as a major hub for clinical trials, manufacturing of generic medicine and increasingly, complex biologics and biosimilar products [5]. These developments necessitate a regulatory infrastructure that can effectively monitor, evaluate, and manage adverse drug reactions (ADRs) both domestically and internationally [6].

The Pharmacovigilance Programme of India (PvPI), which was launched in 2010 by the Indian Pharmacopoeia Commission (IPC), represents the foundation of India's post-marketing safety surveillance system [7]. PvPI coordinates a nationwide network of Adverse Drug Reaction Monitoring Centres (AMCs), collects spontaneous ADR reports, and contributes data to the WHO's global PV database, VigiBase [8]. Over the last decade, PvPI has demonstrated measurable progress in ADR reporting rates, capacity building, and public health interventions [9]. However, various challenges remained, including underreporting by healthcare professionals, limited patient awareness, and resource constraints in rural and semi-urban areas [10].

Global regulatory agencies such as the European Medicines Agency (EMA) and the United States Food and Drug Administration (US FDA) have implemented advanced PV systems that integrate real-world evidence (RWE), electronic health records (EHRs), and artificial intelligence (AI)-based analytics to strengthen safety signal detection [11,12]. These approaches demonstrate the growing role of digital health in pharmacovigilance, offering lessons for India to evolve in the regulatory functioning and strengthening [13]. Comparative assessments between Indian PV regulations, overseen by the Central Drugs Standard Control Organisation (CDSCO), and international regulatory bodies shows both areas of convergence and divergence, particularly concerning generics, over-the-counter (OTC) products, and advanced therapeutics [14, 15].

The integration of post-marketing surveillance (PMS) with real-world data (RWD) sources such as patient registries, claims databases, and social media platforms is emerging as a strategic priority in PV globally [16, 17]. In India, this integration is still at a nascent stage, but ongoing initiatives such as the Ayushman Bharat Digital Mission (ABDM) and interoperability of health information systems indicate a trajectory towards data-driven regulatory decision-making [18, 19].

II. METHODOLOGY

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines to ensure transparency, reproducibility, and scientific rigor. The methodology included the following steps1

2.1 Search Strategy

A comprehensive literature search was performed between 2010 and 2025 using multiple electronic

databases and regulatory websites, including PubMed, Scopus, Web of Science and Google Scholar. Regulatory databases such as CDSCO (India), EMA (Europe), FDA (USA), WHO, IPC, NHA, and government reports were included. Grey literature such as Wikipedia, regulatory guidance documents, and official reports was included. Search terms combined MeSH and free-text keywords, such as: "pharmacovigilance," "drug safety," "PvPI," "CDSCO," "EMA," "comparative frameworks," "real-world evidence," "post-marketing surveillance," "regulatory landscape India," "ADR reporting," and "digital health data."

2.2 Eligibility Criteria and study selection: Studies were included if they:

- Focused on pharmacovigilance systems in India (PvPI).
- Provided comparative analysis of CDSCO and EMA frameworks.
- Discussed integration of real-world evidence (RWE) in pharmacovigilance.
- Included regulatory guidelines, systematic reviews, original research, policy papers, or government/agency reports.

Exclusion criteria: Non-English articles. Studies unrelated to pharmacovigilance or regulatory systems and Case reports, editorials, or opinion pieces without data.

After removal of duplicates (n = 36), 332 titles and abstracts were screened.

- Of these, 198 articles were excluded due to irrelevance.
- 134 full-text articles were assessed for eligibility.
- Finally, after excluding 49 sources due to other reason, a total of 85 sources were included in the review (published research + regulatory documents + guidelines).

2. 3. Data Extraction and Data Synthesis

From each included study, the following data were extracted:

- Study details: author, year, source.
- Domain relevance: India (PvPI), CDSCO–EMA framework, or RWE integration.
- Regulatory scope: national vs. international guidelines.
- Outcomes: strengths, limitations, opportunities, and gaps in PV.

Comparative tables and figures/flowchart were developed to summarize differences between frameworks.

A narrative synthesis was conducted across the three domains.

- Data were categorized under India–PvPI, CDSCO–EMA comparison, and RWE integration.
- Overlapping themes were highlighted (e.g., ADR under-reporting, digital health, post-marketing surveillance gaps).
- Regulatory frameworks were compared using structured tables and visual illustrations.

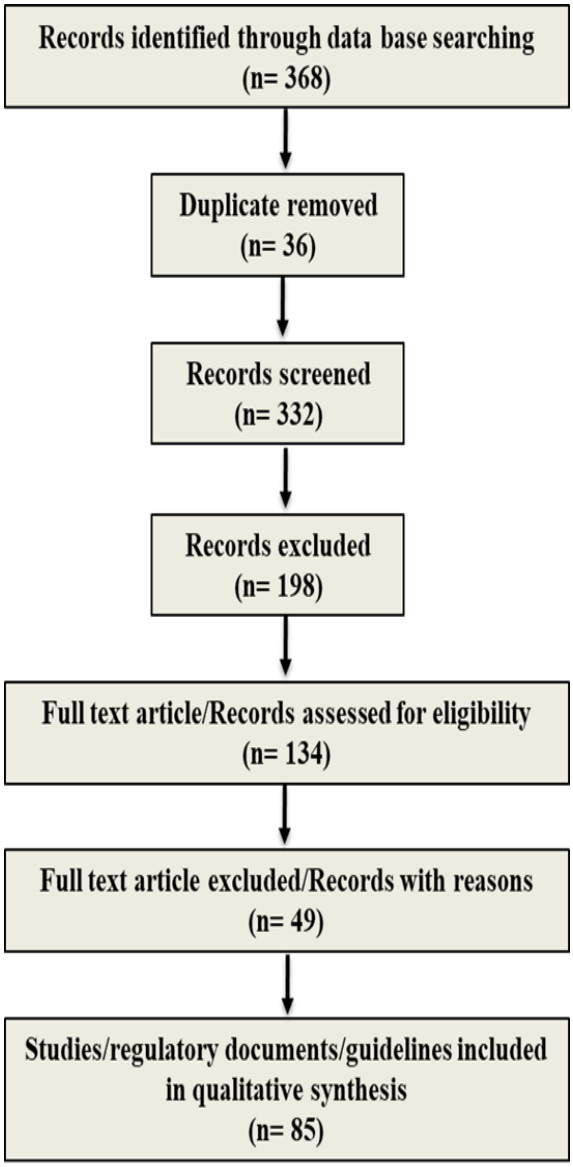

Figure 1 Methodology of literature screening (PRISMA methodology)

III. THE EVOLUTION AND CURRENT LANDSCAPE OF PHARMACOVIGILANCE IN INDIA: CHALLENGES AND OPPORTUNITIES WITH PVPI

3.1 Historical Background

Pharmacovigilance activities in India have evolved significantly over the past two decades, shifting from isolated academic initiatives to a coordinated national programme. India joined the WHO Programme for International Drug Monitoring in 1998, but initial efforts were not significant due to inadequate infrastructure and limited healthcare professionals, consumer and governing body engagement [20]. Recognizing the urgent need for a unified system, the Ministry of Health and Family Welfare launched the National Pharmacovigilance Programme (NPP) in 2004, which was supported by the World Bank under the Health Systems Development Project [21]. While the NPP improved awareness among certain healthcare institutions, it faced challenges in sustainability and coverage, leading to its eventual restructuring [22].

3.2 Establishment of PvPI

In 2010, the Pharmacovigilance Programme of India (PvPI) was officially launched under the Indian Pharmacopoeia Commission (IPC), functioning as the National Coordinating Centre (NCC) [7]. The core objectives of PvPI were as follows:

- Establishing a nationwide network of Adverse Drug Reaction Monitoring Centres (AMCs);
- Collecting and analysing ADR data;
- Disseminating drug safety updates to stakeholders; and
- Contributing to global pharmacovigilance through WHO's VigiBase [8, 23].

  By 2022, PvPI had expanded to include over 500 AMCs across India, integrated within teaching hospitals, tertiary care centers, and select private institutions [24]. These centers collect spontaneous ADR reports from healthcare professionals and patients, which are then validated and coded using WHO Adverse Reaction Terminology (WHO-ART) or MedDRA before being entered into VigiFlow [25].

3.3 Current Operational Framework and Achievements

PvPI operates through a three-tier structure:

1. AMC Level: Initial ADR reporting, validation, and entry into the database.
2. Zonal/Regional Centers: Aggregation, quality control, and training.
3. National Coordinating Centre: Signal detection, causality assessment, regulatory recommendations, and international data sharing [7, 8].

The program covers a range of medicines, including prescription drugs, over-the-counter products, vaccines, and traditional medicines [26]. In recent years, PvPI has also initiated mobile app-based ADR reporting, expanding accessibility to healthcare professionals and consumers [27].

Since inception, PvPI has demonstrated steady improvement in ADR reporting. Between 2011 and 2022, annual report submissions increased from fewer than 5,000 to over 80,000, contributing significantly to India's WHO Global Individual Case Safety Reports (ICSR) share [28, 29]. PvPI data have led to important regulatory actions, including labelling changes, market withdrawals, and safety alerts on drugs such as pioglitazone, nimesulide, and various fixed-dose combinations [30].

The programme has also played a key role in capacity building, conducting regular training workshops for healthcare professionals, pharmacists, and regulatory staff [31]. International collaborations with WHO, Uppsala Monitoring Centre (UMC), and regional PV networks have strengthened India's global standing in drug safety monitoring [8].

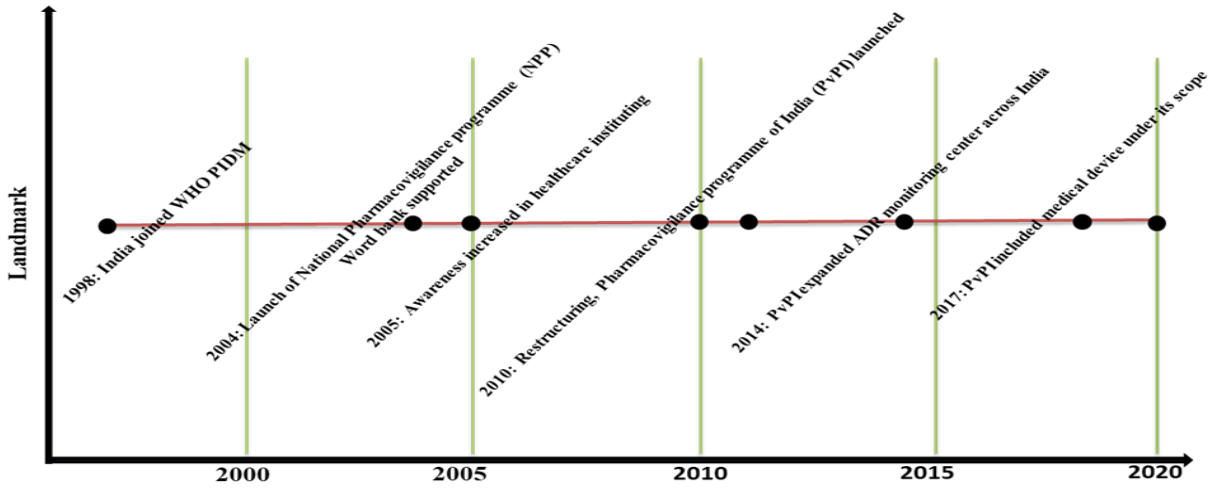

Figure 2 Achieved milestones for Pharmacovigilance industry in India

3.4 Challenges and Opportunities

Despite progress, several challenges continue to limit the effectiveness of PvPI:

- Underreporting of ADRs; Studies suggest that less than 10% of serious ADRs are reported, due to lack of awareness, time constraints, and fear of legal repercussions [32, 33].
- Variable quality of reports; Many ADR reports lack sufficient clinical detail for causality assessment [34].
- Infrastructure disparities; Rural and smaller healthcare facilities often lack trained personnel and reporting systems [35].
- Limited patient involvement; While consumer reporting is permitted, awareness campaigns have not fully reached the general public [36].
- Integration gaps Current PV databases are not fully integrated with EHRs, claims databases, or other real-world data sources [37].

Several strategic opportunities exist for strengthening PvPI:

1. Digital Health Integration Linking PvPI databases with the Ayushman Bharat Digital Mission (ABDM) could enable real-time ADR detection and analytics [18].
2. Artificial Intelligence and Data Mining; Advanced signal detection algorithms, natural language processing, and machine learning can enhance analysis of large datasets[38].
3. Public–Private Partnerships; Collaborating with pharmaceutical companies, technology firms, and academic institutions can expand capacity and innovation [39].
4. Community Engagement; strengthening patient awareness campaigns through mass media, social media, and local health workers [40].
5. Regulatory Harmonization: Aligning PvPI processes with Good Pharmacovigilance Practices (GVP) guidelines used in the EU could improve international credibility and compliance [41].

PvPI has demonstrated that India can operate a large-scale, internationally linked PV programme, but its full potential will only be realized if systemic challenges are addressed alongside strategic adoption of emerging technologies.

IV. COMPARATIVE ANALYSIS OF INDIAN CDSCO AND EMA PHARMACOVIGILANCE FRAMEWORKS: IMPLICATIONS FOR GENERIC AND OTC PRODUCTS

4.1 Overview of Regulatory Authorities and Legal Basis

Pharmacovigilance regulation in India is primarily governed by the Central Drugs Standard Control Organisation (CDSCO), operating under the Drugs and Cosmetics Act, 1940 and the Drugs and Cosmetics Rules, 1945 [42]. PV-specific requirements are detailed in Schedule Y, which mandates post-marketing safety surveillance, adverse event reporting, and risk management for market authorisation holders (MAHs) [43]. The operational arm for national PV

activities is the Pharmacovigilance Programme of India (PvPI) under the Indian Pharmacopoeia Commission [7].

In the European Union (EU), pharmacovigilance is regulated by the European Medicines Agency (EMA) under Regulation (EC) No. 726/2004 and Directive 2001/83/EC, complemented by the Good Pharmacovigilance Practices (GVP) modules [44]. EMA operates EudraVigilance, a centralised database for adverse drug reaction reports from both healthcare professionals and consumers [45]. While CDSCO delegates PV data management largely to PvPI, EMA directly oversees compliance, inspections, and enforcement actions for all MAHs in the EU [46].

4.2 ADR Reporting Requirements, Signal Detection and Risk Minimization

India: MAHs are required to submit Periodic Safety Update Reports (PSURs) every six months for the first two years after marketing approval and annually for the next two years [43]. All serious unexpected ADRs must be reported within 15 calendar days to CDSCO and PvPI [47]. Spontaneous reporting by healthcare professionals is voluntary, although actively encouraged [48].

EU: In contrast, EU legislation mandates that MAHs submit Periodic Safety Update Reports (PSURs) at intervals determined by the EU reference dates list, often in sync with global standards [44]. Serious adverse reactions must be reported within 15 days, while non-serious ADRs are reported within 90 days [45]. Healthcare professionals and patients can report directly to national competent authorities, and reporting is mandatory for MAHs [49].

The EU framework is more prescriptive, requiring electronic submission of ICSRs to EudraVigilance using ICH E2B(R3) format, whereas India is gradually transitioning towards similar electronic standards through VigiFlow [50].

Both India and the EU utilise structured processes for signal detection, causality assessment, and regulatory intervention. However, EMA's GVP Module IX mandates routine signal detection by MAHs using statistical and qualitative methods [44]. EudraVigilance employs Empirical Bayes Geometric Mean (EBGM) and other disproportionality analyses for early detection [51].

In India, signal detection is largely conducted centrally by PvPI, using VigiLyze and other WHO-UMC algorithms [25, 52]. While EMA requires MAHs to implement Risk Management Plans (RMPs) and post-authorisation safety studies (PASS) for certain medicines, India's RMP requirements are still evolving and are not universally applied to generics [53].

4.3 Generic Medicines, Regulatory Considerations and OTC Products Safety Monitoring

The regulatory pathways for generics differ in scope and depth between India and the EU.

- India: Generics are approved primarily on the basis of bioequivalence data without extensive clinical safety evaluation [54]. PV obligations for generics are similar to those for innovator products, but proactive risk minimisation is less systematically enforced [55].
- EU: Generics undergo bioequivalence testing, but MAHs must also implement full PV systems, maintain a Qualified Person responsible for PV (QPPV), and submit RMPs where safety concerns exist [44, 56].

This difference means that post-marketing safety data for generics in India may be less comprehensive, especially in the early post-launch period.

Over-the-counter medicines present unique challenges in PV due to widespread use without medical supervision.

- India: Regulatory oversight for OTC medicines is relatively underdeveloped, with no formal, publicly available list of approved OTC products [57]. ADR reporting for OTC drugs is integrated into the general PvPI system, but consumer awareness is low [58].
- EU: EMA and national authorities maintain structured lists of OTC products, with specific labelling and safety monitoring requirements [44]. Patient reporting is actively promoted, and safety communications for OTC drugs are frequently disseminated [59].

This regulatory gap in India could lead to under-detection of safety issues for widely used self-medication products.

4.4 Gaps and Harmonization Opportunities

Several areas present opportunities for alignment between CDSCO and EMA PV frameworks:

1. Mandatory Healthcare Professional Reporting: India could benefit from legal mandates for ADR

reporting by health care providers, similar to certain EU countries [44].

2. Enhanced Risk Management: Expanding the use of RMPs to generics and OTC products in India would align safety planning with EU standards [53].
3. Consumer-Centric PV: Greater promotion of patient reporting, simplified digital tools, and public safety alerts could improve OTC monitoring [60].
4. Electronic Data Interoperability: Harmonisation with ICH E2B(R3) standards for all PV reporting would streamline international data sharing [50].
5. Regulatory Inspections: Strengthening PV inspections for MAHs could enhance compliance and quality assurance [61].

The EMA model demonstrates that robust PV systems depend on integrated reporting obligations, active surveillance, and a culture of transparency. While India has made notable strides through PvPI, further regulatory refinements could enhance its capacity to monitor the safety of generics, OTC medicines, and innovative therapies on par with international best practices.

Table 1 Comparative Analysis: CDSCO vs EMA PV Frameworks (Generics & OTC)

Dimension	India (CDSCO/PvPI)	EU (EMA/EudraVigilance)	Implications (Generics)	Implications (OTC)
Regulators & Legal Basis	CDSCO under Drugs & Cosmetics Act, 1940 and Rules, 1945; PV in Schedule Y. PvPI (IPC) as operational arm.	EMA under Reg. (EC) 726/2004 & Dir. 2001/83/EC; detailed GVP Modules; central EudraVigilance DB.	India relies on PvPI; oversight less centralised than EMA variability in MAH compliance.	Less prescriptive oversight vs EU; fewer structured consumer-facing obligations.
ADR Reporting Requirements	PSURs: q6 months (first 2y), then annually (next 2y). Serious unexpected ADRs in 15 days. HCP spontaneous reporting voluntary.	PSURs per EU reference dates; serious ADRs in 15 days; non-serious in 90 days; MAH reporting mandatory; HCP/patient direct reports allowed.	EU's mandatory, electronic ICSR reporting standardizes coverage; India transitioning via VigiFlow.	EU enables direct patient reporting → richer OTC safety data; India's voluntary HCP reporting limits signal volume.
Electronic Standards	Gradual transition to electronic standards via VigiFlow; WHO-UMC ecosystem.	Mandatory ICH E2B(R3) electronic ICSRs to EudraVigilance.	EU interoperability supports rapid cross-market signal sharing; India catching up.	Better electronic capture in EU improves OTC signal detection latency.
Signal Detection & Risk Minimization	Central PvPI signal detection using VigiLyze/WHO-UMC algorithms; RMPs evolving, not universal for generics.	GVP Module IX: routine MAH signal detection; EBGM & disproportionality analyses; RMPs & PASS required where applicable.	EU demands MAH-led analytics + RMPs → stronger early post-launch oversight; India more centralised, variable RMP use.	EU's structured minimisation (labelling/education) more established; India's measures developing.
Generics – Regulatory Considerations	Approval mainly via bioequivalence; PV obligations similar to innovators but proactive minimisation less systematic.	Bioequivalence + full PV system; QPPV mandatory; RMPs when safety concerns exist.	India may have less comprehensive early post-marketing safety data; EU requires mature PV systems at launch.	Stronger EU PV systems benefit Rx-to-OTC switches where applicable.
OTC Safety Monitoring	No formal public OTC list; OTC ADRs via PvPI; low consumer awareness.	Structured OTC lists and labelling; active patient reporting and frequent safety communications.	—	EU more likely to detect OTC safety issues earlier; India risk of under-detection.
Inspections & Enforcement	PV inspections strengthening; CDSCO delegates data ops to PvPI.	EMA/National authorities oversee compliance, inspections, enforcement for all MAHs.	EU inspections pressure MAHs to maintain robust PV for generics.	Better compliance culture supports OTC safety actions in EU.
Gaps & Harmonisation Opportunities	Mandate HCP reporting; broaden RMPs to generics/OTC; promote patient reporting; align to E2B(R3); strengthen inspections.	Integrated obligations, active surveillance, transparency as reference model.	Alignment would enhance generics' post-marketing evidence quality.	Consumer-centric PV + interoperability would raise OTC signal capture.

V. INTEGRATION OF REAL-WORLD EVIDENCE AND POST-MARKETING SURVEILLANCE IN INDIAN PHARMACOVIGILANCE: A REGULATORY PERSPECTIVE

5.1 Defining Real-World Evidence and Its Relevance to PV and Current Status of RWE Use in India's PV System

Real-world evidence (RWE) refers to clinical evidence regarding the usage, benefits, and risks of a medical product derived from the analysis of real-world data (RWD), such as electronic health records (EHRs), insurance claims, registries, and patient-generated data [62, 63]. The U.S. FDA defines RWE as "the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of real-world data" [64]. In pharmacovigilance, RWE complements traditional spontaneous reporting by enabling active surveillance, signal validation, and long-term safety assessment [65].

Globally, regulatory bodies like the FDA and EMA have embraced RWE as part of drug safety decision-making. The FDA's Sentinel Initiative and EMA's EudraVigilance and EU PAS Register demonstrate how structured RWD sources can enhance post-marketing surveillance [66, 67]. For India, where the healthcare system is heterogeneous and fragmented, RWE integration offers an opportunity to bridge existing gaps in ADR detection and reporting [68].

India's pharmacovigilance ecosystem is still heavily reliant on spontaneous ADR reporting through PvPI, with limited integration of structured RWD sources [7, 69]. A few initiatives hint at progress:

- Hospital EHR Pilots: Select tertiary hospitals have linked ADR reporting modules with hospital information systems [70].
- Disease Registries: Oncology and rare disease registries managed by research institutions have been used sporadically for safety signal analysis [71].
- Mobile App ADR Reporting: PvPI's "ADR PvPI" app allows healthcare providers and patients to submit ADRs digitally [27].

However, large-scale, systematic integration of RWE into regulatory PV processes remains limited, hindered by infrastructural, legal, and data quality challenges [72].

5.2 Challenges to RWE Integration in Indian PV and Opportunities and Enablers

Several systemic barriers impede the effective use of RWE in India's post-marketing safety monitoring:

1. Fragmented Health Data Systems: Patient health data are dispersed across public and private providers with limited interoperability [73].
2. Data Quality and Standardization Issues: Inconsistent coding, incomplete records, and lack of MedDRA adoption across all systems reduce analytical reliability [74].
3. Privacy and Legal Concerns: The Digital Personal Data Protection (DPDP) Act, 2023 mandates strict consent requirements, posing operational challenges for large-scale RWD use [75].
4. Limited Analytical Capacity: Regulatory and PvPI staff often lack specialized training in advanced analytics, AI, and big data processing [76].
5. Underdeveloped Active Surveillance Infrastructure: India lacks a national-level active monitoring network comparable to FDA Sentinel [66].

Despite these challenges, India is positioned to make significant advances in RWE integration:

- Ayushman Bharat Digital Mission (ABDM): This nationwide initiative aims to create interoperable digital health infrastructure, potentially enabling linkage between EHRs, PV databases, and health registries [18,77].
- Artificial Intelligence and Natural Language Processing (NLP): AI algorithms can mine unstructured text from clinical notes, social media, and literature to identify emerging safety concerns [78].
- Social Media and Patient-Generated Data: Platforms such as Twitter, Facebook, and disease-specific forums can be mined for patient-reported ADRs, complementing formal reports [79].
- Linkage with Insurance Claims Data: India's expanding health insurance coverage under schemes like PM-JAY could provide longitudinal drug utilisation and safety data [80].
- International Collaboration: Learning from EMA's PASS model and FDA's Sentinel methods could accelerate development of India-specific frameworks [81].

5.3 Proposed Framework for RWE-Driven PMS in India:

An integrated RWE–PMS system for India could adopt a hybrid surveillance model combining spontaneous reporting with active data monitoring:

1. Data Source Integration: Link PvPI, EHRs, registries, and claims databases under ABDM interoperability standards.
2. Analytical Hub: Establish a central data analytics unit within PvPI equipped with AI/ML capabilities for signal detection [82].
3. Regulatory Guidance: CDSCO to issue RWE-specific PV guidelines aligned with ICH E2E and EMA's PASS framework [44, 83].
4. Stakeholder Training: Upskill regulators, healthcare providers, and data scientists in RWE methodologies [84].
5. Pilot Programs: Implement disease-specific active monitoring pilots before nationwide rollout.

5.4 Global Best Practices Applicable to India:

- FDA Sentinel Initiative: Demonstrates scalable active safety surveillance through distributed data networks [66].
- EMA PASS Studies: Ensure proactive risk assessment and post-authorisation safety measures [44].
- Japan's MID-NET: Integrates hospital EHRs into national safety monitoring, offering a model for India's tertiary care network [85].

India's regulatory evolution towards RWE-driven PMS will require legal clarity, technical interoperability, and sustained investment. If effectively implemented, such integration could transition the country from a largely reactive PV system to a proactive, data-driven safety monitoring framework

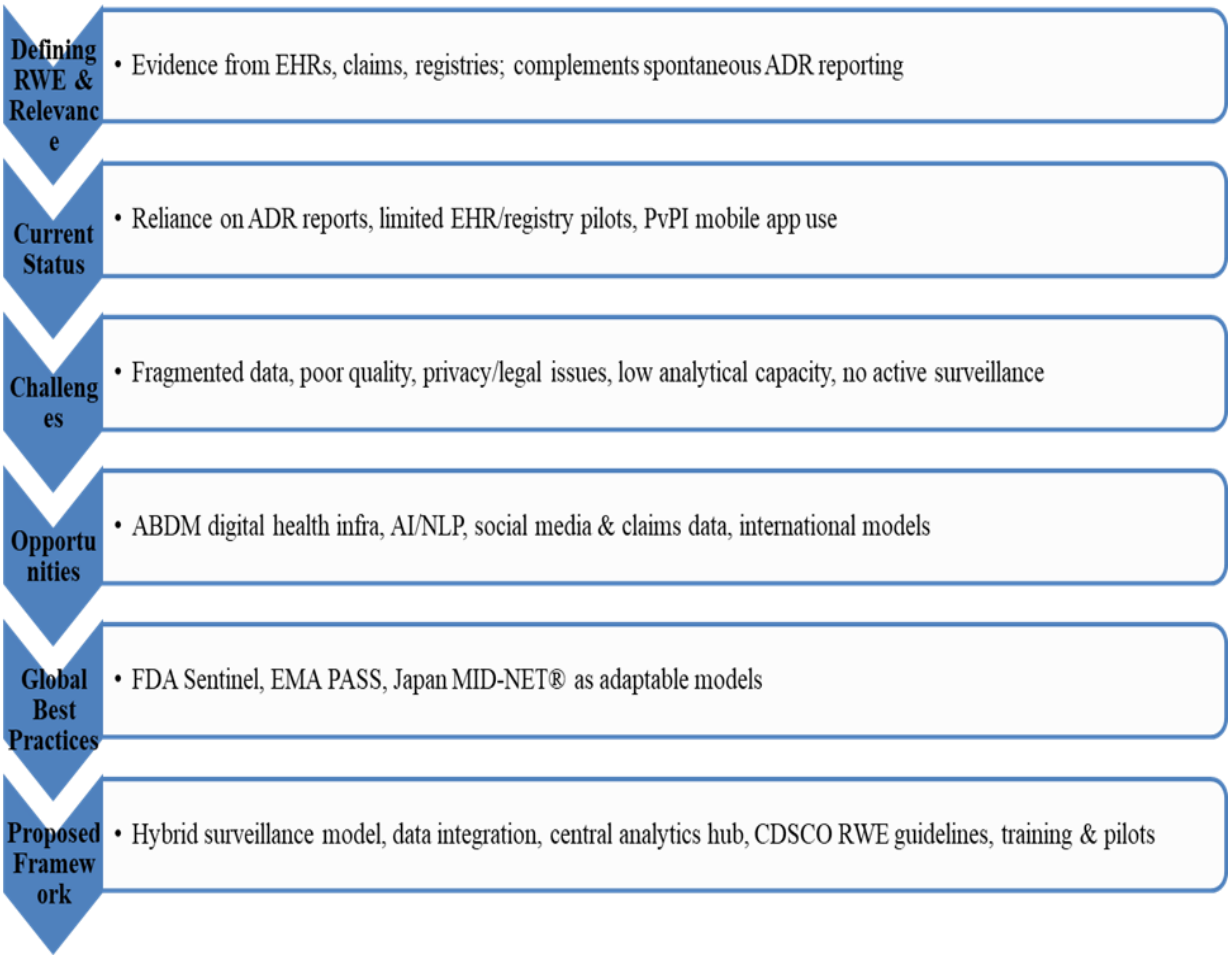

Figure 3: Integration of RWE and PMS in Indian Pharmacovigilance

VI. DISCUSSION AND FUTURE PERSPECTIVE

India's pharmacovigilance (PV) ecosystem has undergone a significant transformation in recent years, with the Pharmacovigilance Programme of India (PvPI) serving as the backbone for drug safety monitoring. The establishment of Adverse Drug Reaction Monitoring Centres (AMCs), capacity-building initiatives, and regulatory interventions have strengthened the framework. Nevertheless, challenges such as persistent underreporting, variable quality of case reports, limited patient engagement, and infrastructural disparities across states restrict the system from achieving its full potential. These issues reflect not only systemic limitations but also cultural and educational barriers that need to be addressed through broader stakeholder engagement.

The comparative analysis of CDSCO and EMA frameworks highlights India's commendable progress in aligning with global regulatory standards. While both share common principles such as risk assessment, post-marketing surveillance, and patient safety focus the EMA system demonstrates stronger enforcement of Good Pharmacovigilance Practices (GVP), mandatory reporting requirements, and robust risk management planning. Addressing these gaps in India is essential for strengthening domestic PV while simultaneously enhancing India's credibility as a global pharmaceutical leader.

Looking ahead, the integration of Real-World Evidence (RWE) offers a transformative pathway. With the expansion of electronic health records, patient registries, insurance claims databases, and novel data sources such as social media, RWE can complement spontaneous reporting by generating proactive safety insights. National initiatives like the Ayushman Bharat Digital Mission (ABDM), supported by artificial intelligence and big data analytics, can play a pivotal role in strengthening active surveillance mechanisms. However, this requires robust data governance frameworks, interoperability across systems, and investments in training pharmacovigilance professionals and data scientists to manage complex datasets.

Future perspectives suggest that India should adopt a multipronged strategy: strengthening regulations by updating Schedule Y to explicitly include RWE guidance, integrating PvPI with national health platforms to enable real-time signal detection, and fostering a culture of safety reporting among healthcare professionals and patients. Additionally, active collaboration with global regulators such as EMA, FDA, and WHO will be critical in harmonizing practices and achieving interoperability. By adopting these measures, India's PV system can transition from a reactive and compliance-driven model to a predictive, technology-enabled, and globally harmonized safety ecosystem.

VII. CONCLUSION

Pharmacovigilance has emerged as a cornerstone of patient safety in India's growing pharmaceutical landscape. The development of PvPI and its expanding scope signify progress toward establishing a robust drug safety system. However, challenges related to underreporting, inconsistent ADR data quality, and insufficient patient engagement persist.

Comparative insights with the EMA framework reveal that while India is moving in the right direction, regulatory harmonization, stronger enforcement of GVP, and mandatory reporting remain pressing needs. The integration of RWE and post-marketing surveillance enabled by digital health platforms, artificial intelligence, and national initiatives like ABDM provides a timely opportunity to elevate India's pharmacovigilance standards.

In essence, India stands at a pivotal juncture. With strategic policy reform, technological integration, and global alignment, the country has the potential to transform its pharmacovigilance system into a proactive, predictive, and internationally harmonized model. Such advancements will not only safeguard domestic public health but also consolidate India's reputation as a trusted contributor to global drug safety

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