

patient centrality in pharmacovigilance: new directions and new horizons for transformation

Supriya Desai

The importance of pharmacovigilance (PV) as a science, critical to both effective patient care in clinical practice and public health is growing. Patient-centeredness and patient safety have emerged as core elements in today's interactive and responsive healthcare systems. As patients take more interest in their health and healthcare, they support the maxim of "Nothing about me, without me" and expect caregivers to engage in shared decision making, so that the patients' voice is always included.

Patients usually report adverse drug reactions (ADRs) to their doctors. However, since only 5% of doctors are estimated to participate in PV, traditional mechanisms may not be efficient in ensuring adequate safety reporting. Data from studies indicate that systems which enable direct recording of patient concerns may identify new drug safety signals earlier than professional reporting systems alone¹. This emphasises that the patients' role in actively reporting ADRs is key to building a better PV ecosystem.

Public health programmes and responsible media coverage aimed at increasing access to drug information has led patients in many countries to take greater responsibility for their own health. This is reflected in the creation of patient charters, patients' bills of rights² and patient advocacy groups. For example, patients with HIV/AIDS have been instrumental in creating international awareness of disease impact, improving access to therapies and communication of associated medication risks.

Patient-centric innovation will be at the heart of the transformation of PV over the next couple of decades and this will likely forever change PV as we know it today. But are we really prepared to implement patient-centric approaches in PV? What steps are required to bring safety to patients, as opposed to bringing patients to safety?

Patient-centred implementation in PV

In Europe, the EU Directive 2010/84/EU and EU Regulation No. 1235/2010 provide recommendations, developed by the European Patients' Forum, for patient-centred implementation for PV. These recommendations are intended to lead to a strong, open and transparent PV system that ensures the confidence of patients, healthcare professionals (HCPs) and regulators alike and represents a step forward for safe, high quality and patient-centred healthcare^{3,4}.

The Directive 2010/84/EU amends the definition of ADRs to include medication errors and misuse as part of ADR reporting to help collect more information on the real-life working of medicines, when used in different circumstances by different people. Products, subject to additional monitoring (e.g. products with new active substances, biologics) need to be identified by a black symbol with a standard explanatory sentence on the packaging indicating that the medicine is under additional monitoring, what such monitoring means and the reasons behind it, without creating unwarranted alarm so that patients do not stop their treatment unnecessarily. This transparency is paramount to ensure patients' trust in the functioning of the PV system.



Supriya Desai MD, PGDBM is a Clinical Research and Pharmacovigilance (PV) Executive with over 16 years of experience in clinical practice and in various leadership roles in the healthcare industry including clinical research, drug safety and PV. In her current role as Medical Director and Practice Head at Sciformix, she provides scientific and operational leadership to a global medical team (across India, Philippines and US); involved in medical review activities across pharmacovigilance, safety writing, signal management and allied safety surveillance activities, spanning diverse therapeutic areas.



The shift from pure safety analysis to benefit–risk evaluation and thereby the overall implementation approach for an effective patient-centric PV model is entrenched in four main steps; namely to educate, encourage, engage and enable patients, as outlined in **Figure 1**.

Step 1: Education and encouragement

One of the key approaches in patient-centric PV is raising patient awareness regarding the importance of reporting ADRs and continually highlighting the critical role they can play in PV, right from safety reporting through risk communication.

Targeted educational initiatives include training programmes to directly train consumers and patients regarding adverse event (AE) reporting systems, as well as train investigator site teams, patient organisations and HCPs. Dissemination of product safety summaries, benefit–risk data and risk management plan summaries for public consumption on a real-time basis is important and can be through company websites, national web portals and patient information

centres. Medical concepts need to be comprehensively communicated in an understandable and accessible format to patients. Involvement of patient organisations as experts for development of safety information as well as for set-up and development of the national web portals on medicines is critical.

The growing commercial relevance of emerging markets coupled with lower levels of patient awareness in these regions poses a specific challenge and would likely limit the success of patient-centric measures in a global PV environment. In this context, involving HCPs like pharmacists, nurses or physicians builds upon existing relationships between providers and patients and helps activate their patients to participate in safety reporting activities. Reported information can be acted upon by the HCP or reported to other HCPs, as appropriate and provides a mechanism for providers to report complementary clinical information or enable linkage to a medical record. Direct appreciation and recognition for patient efforts to report AEs with possible provision of some incentives (non-monetary) to patients and consumers would further encourage ADR reporting.

Step 2: Engage purposefully and enable proactively

ADRs are estimated as the fifth largest cause of deaths in hospitals⁴, yet only around 10% to 25% of all ADRs are reported. Underreporting of ADRs is a serious issue, which undermines the evaluation of safety of medicines. Direct patient participation in reporting drug-related problems can increase the efficiency of the PV system and compensate for some of the shortcomings of systems based on HCP reports only⁵.

The Directive 2010/84/EU [Article 102(b)] proposes guidance encouraging direct patient reporting of ADRs, via appropriate measures including web-based and alternative formats to the national competent authorities (NCAs). Studies show that patient reports are more valuable compared to HCP reports as patients often report earlier, perceive the impact and severity of reactions differently and give more detailed descriptions, including specific circumstances in which the reaction occurred. In certain situations, like ADRs resulting from prescribing errors or off-label use of medications and ADRs of intimate nature,

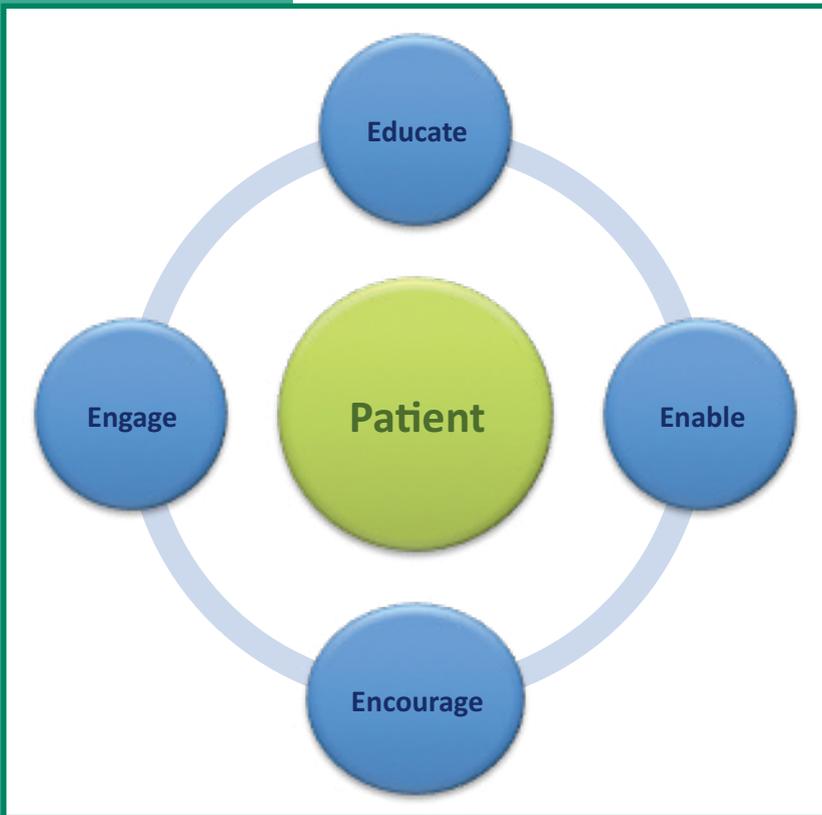


Figure 1: Implementation model for patient-centric pharmacovigilance.

direct reporting by patients would enable collection of such crucial safety data to ensure better medication safety⁶.

Patient-reported outcomes (PROs) are data elements directly reported by patients about experiences with healthcare, symptoms, functional status, or quality of life⁷. The Patient Reported Outcomes Safety Event Reporting (PROSPER) Consortium comprises of industry, regulatory authority, academic, private sector and patient representatives interested in the area of patient reported outcomes of adverse events (PRO-AEs). This consortium has put forth specific guidance for improved safety reporting by better incorporation of the patient's 'voice' and perspectives into collection of safety data, so that the safety profile and benefit–risk balance of new and existing medicines is better defined⁸.

Effective involvement of patients in the AE reporting process is possible by use of novel ADR reporting tools and processes like ADR online forms, mobile applications and through local pharmacies. Further, patient involvement in set-up and user-testing of the reporting systems ensures that the system is fit-for-purpose and user-friendly. Developing guidelines for the follow-up procedure for reports in consultation with patient and HCP organisations enables collection of high-quality data, conveys feedback to patients on how the information will be used and provides patients with further information or where information is available (e.g. the publicly-accessible part of the EudraVigilance database³).

Engaging patients as partners in the data collection enterprise would enable systematic collection of information and provide a more comprehensive picture within a population. This can be achieved in limited populations via patient registries, or in a wider population using existing infrastructure to engage patients, e.g. community pharmacies and pharmacists⁹.

Additional patient-centred PV initiatives include real-time monitoring of clinical trial safety data with targeted back-up data collection methods to reduce missing data for non-compliant patients (e.g. electronic reminders, email, telephone or a human call). Collection of patient reports via approaches linked to electronic health records, clinical

practice records and pharmacy registries within national health systems (containing confirmed patient-level health and treatment information) would provide the ability to link validated patient information (around diagnosis, co-morbidities, allergies and other treatments) for analysis of aggregated safety data, and help better understand the etiology of rare reactions and possible correlation of patient-related genomic data with specific safety issues¹⁰.

Social media offers another novel channel for driving patient-centric PV. Most social media activities for PV by companies are focused on screening of social media sites to ensure adequate safety reporting. Easy, convenient reporting of AEs via simple patient-friendly mobile applications (deployed on mobiles, smartphones), monitoring of company-managed websites, health forums and monitoring of safety data reported on social media sites like Facebook and Twitter are useful in this context¹¹.

Patient engagement in the PV process can only be considered truly complete when the patients and the public are involved in the risk management and communication process. The industry, regulators and HCPs must build public trust through effective risk communication by proactively publishing required safety information as per EU guidance. High-quality information empowers patients to play their role in the PV system, to drive better patient safety and high quality of care^{5,6}.

EU Directive 2010/84/EU [Chapter 2 of title IX] contains crucial provisions from the patients' perspective concerning transparency and communication regarding medicines, while Articles 21 and 106 list information that NCAs should make publicly available through national web portals. This includes marketing authorisation, assessment reports, package leaflets, summary of product characteristics, risk management plan summaries, list of medicinal products subject to additional monitoring, and information on different ways of reporting ADRs to the NCA by HCPs and patients. Further, involvement of patients and patient organisations in testing of patient information leaflets and other safety information prior to release per mandatory (readability) user testing in the





EU and use of the US Food and Drug Administration's (FDA's) new Physician Labelling Rule format for display of important risk information for patients are required. Another recommendation [Section 4, Chapter 3 of the Pharmacovigilance title (Article 107i to k)] requires Member States to involve and consult patient organisations and HCPs as appropriate to provide the right messages, advice in case of urgent safety measures such as suspensions or recalls, and employ appropriate temporary measures^{3,4}.

Social media can also serve as an effective digital tool for risk management and communication for PV teams within companies to directly connect and engage with patients, consumers and HCPs to improve awareness about product safety, leading to improved health literacy amongst consumers and patients, as shown in **Figure 2**¹¹.

Today, patients in the US depend on prescription and over-the-counter medications to sustain their health, with 3 billion prescriptions written annually. The Institute of

Medicine estimates that at least 1.5 million preventable ADRs, including medication misuse occur within the healthcare system each year¹². The goal of the US FDA Safe Use Initiative is to create and facilitate public and private collaborations within the healthcare community to reduce preventable harm by identifying specific, preventable medication risks and developing, implementing and evaluating cross-sector interventions with partners who are committed to safe medication use^{13,14}.

The label is the patient's best, and often only, source of information. It is the safety net to prevent medication errors. While written information and oral consultations may sometimes be available, the prescription container label must be able to fulfil the professional obligations of physicians and pharmacists to give the patient all the information needed to understand how to safely use the medication. The recommendations made by the US Pharmacopeia Health Literacy and Prescription Container Labelling Advisory Panel in November 2009¹⁴ outline multiple patient-

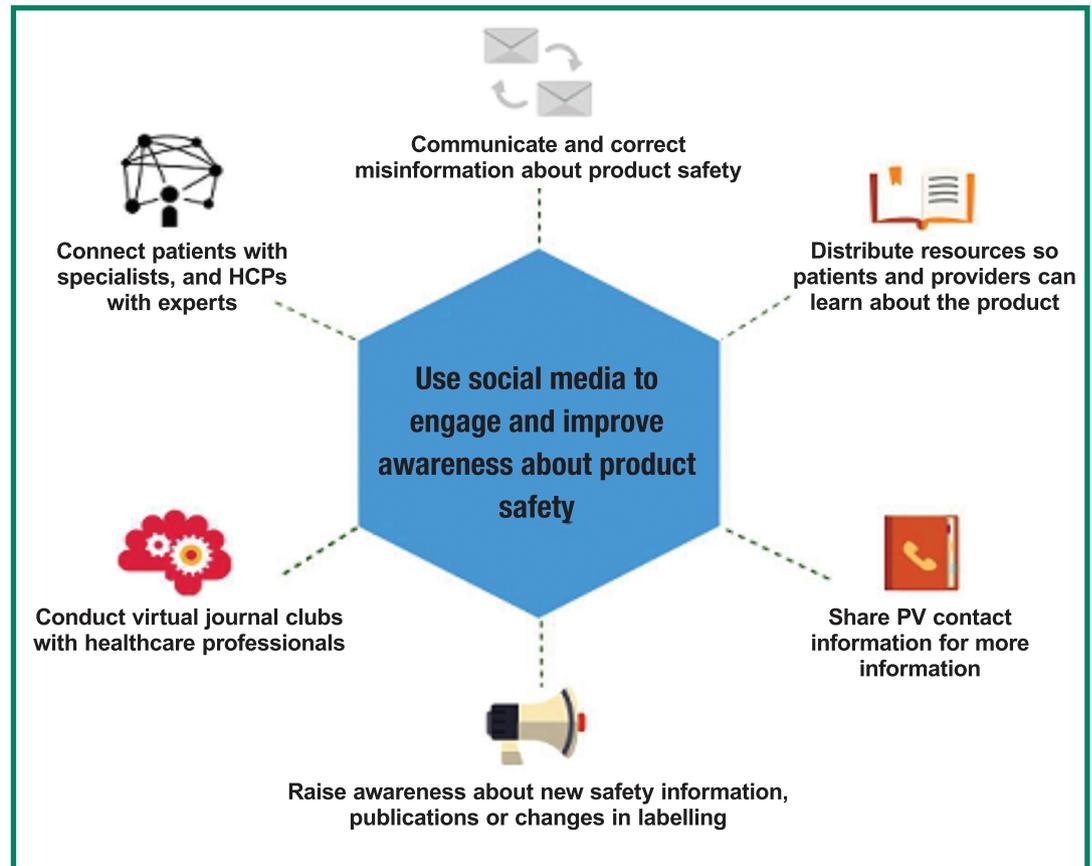


Figure 2: Using social media to engage patients and improve awareness about product safety.

centric labelling measures to reduce preventable ADRs. These include the following.

1. Organise prescription label in a patient-centred manner.
2. Simplify label language.
3. Use explicit text to describe dosage/interval instructions.
4. Include purpose for use on label.
5. Improve label readability.
6. Provide labelling in patient's preferred language, include supplemental information on label and standardise directions.

Summary

The patient perspective is an essential component of the drug safety monitoring and risk communication process. PV organisations that incorporate the patients' 'voice' in PV systems and processes would be better positioned over the long-term to ensure patient safety and add real value back to the patients by enhancing product benefit-risk profiles. Overall, adopting a patient-centric approach and partnering with patients and public for reporting, analysis and communication of safety data seems to be the way forward.

At the same time, it is critical to remember that patient centricity is more about listening, communicating and disseminating to the patients, to ultimately empower them to participate in the decision-making process and not about putting the decision-making solely in their hands. The public has increasingly influenced HCP prescribing and patterns of drug use in recent years due to increased reach of the media and internet. Furthermore, direct advertising to consumers of prescription medicines has become commonplace in many countries. With this information, patients feel more empowered to make their own therapeutic decisions, without assistance from HCPs, resulting in increasing self-medication, over-prescribing by doctors on patients' demand and misuse of medications^{15,16}.

Variations in the way medicines are used can potentially alter their safety profiles and these need to be investigated further. In addition, it needs to be determined how access to drug information can influence patient safety, including patients' perception of safety and the level of harm patients are prepared to

accept for different medicines. The outcome of such research would be the creation of better formulated policies within the evolving patient-centric models with the goal to reduce patient risk².

References

1. Egberts GPG, Smulderes M, De Konig FHP, et al. Can adverse drug reactions be detected earlier? A comparison of reports by patients and professionals. *British Medical Journal* 1996;**313**:530–531.
2. De Vries CS, Duggan CA, Tromp TFJ, de Jong-van den Berg LTW. Changing prescribing in the light of tolerability concerns: how is this best achieved? *Drug Safety* 1999;**21**(3):153–160.
3. European Patients' Forum. *Directive 2010/84/EU and Regulation (EU) No 1235/2010. Amending the EU Pharmacovigilance Legislation Recommendations for a Patient-Centred Implementation*. Brussels, Belgium: European Patients' Forum; April 2012. <http://www.eu-patient.eu/globalassets/policy/pharmaceuticalpackage/pharmacovigilance-recommendations-for-patient-centred-implementation.pdf>. Accessed 28 June 2015.
4. European Commission. *Questions & Answers: Pharmacovigilance*. Belgium, Brussels: European Commission; 31 December 2010. http://ec.europa.eu/health/files/pharmacovigilance/qa_pharmacovigilance_2011_en.pdf.
5. Consumer reporting of ADRs. *WHO Drug Information* 2000;**14**:211–215.
6. Lloyd AJ. The extent of patients' understanding of the risk of treatments. *Quality in Health Care* 2001;**10** Supplement 1:14–18.
7. Basch E. New frontiers in patient-reported outcomes: adverse event reporting, comparative effectiveness and quality assessment. *Annual Review of Medicine* 2014;**65**:307–317.
8. Banerjee AK, Okun S, Edwards IR, et al. Patient-Reported Outcome Measures in Safety Event Reporting: PROSPER Consortium Guidance. *Drug Safety* 2013;**36**:1129–1140.
9. Leone R, Moretti U, D'Incau P, et al. Effect of pharmacist involvement on patient reporting of adverse drug reactions: first Italian study. *Drug Safety* 2013;**36**(4):267–276.
10. Basch E. Systematic collection of patient-reported adverse drug reactions: a path to patient-centred pharmacovigilance. *Drug Safety* 2013;**36**(4):277–278.
11. Desai S. Social media for drug safety: navigating the evolving, complex global regulatory ecosystem. *PharmaAsia*; 14 August 2015. <http://www.pharmaasia.com/article/social-media-for-drug-safety-navigating-the-evolving-complex-global-regulatory-ecosystem/11921>
12. Institute of Medicine of the National Academies. *Preventing Medication Errors*. Washington, DC, USA: National Academies Press; 2007, p. 124.
13. FDA. *Safe Use Initiative Fact Sheet*. Silver Spring, MD, USA: FDA; 5 June 2014. <http://www.fda.gov/Drugs/DrugSafety/ucm188760.htm>
14. Institute of Medicine of the National Academies. *The Safe Use Initiative and Health Literacy – Workshop Summary*. Washington, DC, USA: National Academies Press; 1 December 2010. <http://www.iom.edu/Reports/2010/The-Safe-Use-Initiative-and-Health-Literacy-A-Workshop.aspx>
15. Schwartz RK, Soumerai SB, Avorn J. Physician motivation for non-scientific drug prescribing. *Social Science and Medicine* 1997;**44**(4):541–548.
16. Sachs L, Tomson G. Medicines and culture – a double perspective on drug utilization in a developing country. *Social Science and Medicine* 1992;**34**(3):307–315.

