

SAFETY ANALYSIS INSIGHT

Enhancing Patient Involvement in Spontaneous Reporting

Insights from VigiBase Data Analysis and Proposed Strategies for Improved Engagement

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Introduction

In the previous decade, patient participation in healthcare has grown significantly, to the extent that the concept of 'patient centricity' has become a prevalent theme in all activities related to patients. In the evolving context, patient involvement in pharmacovigilance has been limited, partly due to the perception that adverse event management is best suited for healthcare professionals and a lack of encouragement for active patient engagement.¹ A review of patient-centered pharmacovigilance from 2018 emphasized the necessity for enhancing patient awareness regarding adverse drug reaction (ADR) reporting.²

Historically, pharmacovigilance prioritized the detection and reporting of serious side effects, facilitated by robust systems. However, as more drugs receive expedited approvals based on smaller trials, the need for accurate post-approval adverse event reporting becomes vital, especially in light of the growing significance of real-world evidence in regulatory evaluations.^{1, 3} This suggests that patients' reports detailing their experiences with new drugs, including minor adverse events, may play an increasingly significant role in regulatory decisions.¹ This is particularly pronounced when considering the rising importance of minor adverse events to patients, as these events directly affect their quality of life.¹ Simultaneously, doctors frequently lack the time to report them and may underestimate the impact of minor side effects on patients' well-being.¹

Patients' reports tend to emphasize the subjective impact of adverse events, whereas reports from healthcare professionals contain substantial clinical data but often lack insight into the patient's experience.⁴ Patients reporting provide detailed descriptions of ADRs, encompassing diverse drugs and system organ classes, distinguishing it from healthcare professional reporting.⁵ However, it's worth noting that patient reporting remains relatively infrequent across most countries.⁵

The primary goal of the spontaneous reporting system is to swiftly identify new, rare, and severe ADRs. It⁶ holds the advantage of efficiently encompassing the entire population.⁷ Including patients formally in spontaneous reporting aligns with the current drive for a more engaged pharmacovigilance system.⁸ Enlisting medicine users in this process could potentially address underreporting and identify new risks within specific patient groups.⁷

The aim of this study is to advance the integration of patients' active participation in spontaneous reporting systems by leveraging insights from an analysis of VigiBase data. Through an examination of patient engagement patterns and their impact on reporting, the study seeks to propose strategies for enhancing patient involvement, ultimately contributing to improved engagement and more comprehensive pharmacovigilance efforts.

Methodology

The Oracle Health Sciences Empirica Signal application was used to retrieve the source. VigiBase, the WHO global database of reported potential side effects of medicinal products, developed, and maintained by the Uppsala Monitoring Centre was selected as the primary data source to assess the involvement of patients in the spontaneous reporting of adverse events.⁹ As the classification of patients as reporters is unavailable in VigiBase, the engagement of customers was evaluated through this article. This approach was adopted due to the inclusion of patients within the category of reporters in this context.

Case series were created using database queries. Cumulative data was retrieved for all spontaneous reports, irrespective of the event terms and suspect drugs, with 2022Q4 cut-off dates. Initially, deduplicated spontaneous case reports were presented per reporter, enabling an assessment of the global participation of customers in spontaneous reporting. Subsequently, these spontaneous cases were sorted according to their region of origin and reporter, facilitating an evaluation of customer involvement in spontaneous reporting across various geographic areas.

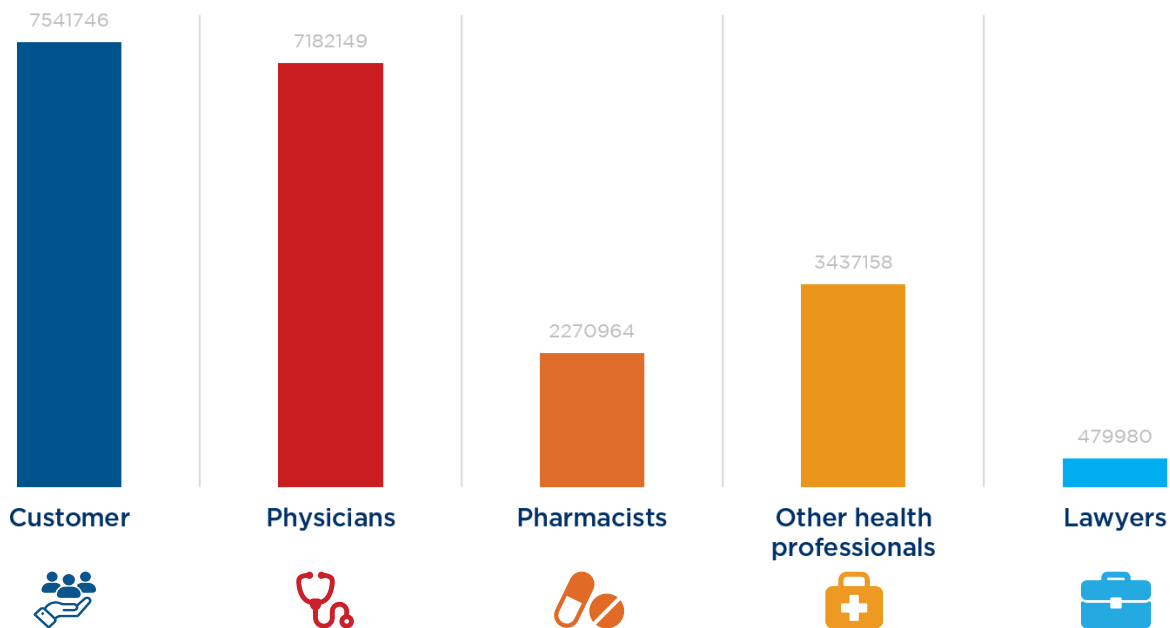
Furthermore, a brief literature search was undertaken to identify the prevailing factors and actions taken by the regions with the highest customer involvement in spontaneous reporting.

Additionally, all spontaneous cases were categorized by age group, focusing on the most prevalent groups of reporters—customers and physicians. Additionally, an evaluation was conducted solely on serious cases categorized by reporter, aiming to ascertain if similar reporting patterns were observed for such cases.

Results and Discussion

Case series were retrieved using database queries, following the criteria outlined previously. **The cumulative presentation of worldwide spontaneous case reports by reporter is depicted in Figure 1.** Customers emerged as predominant reporters overall (in 7,541,746 cases), followed by physicians (7,182,149), other health professionals (3,437,158) and pharmacists (2,270,964). Comparatively fewer reports were contributed by lawyers (479,980).

Figure 1. Distribution of Global Spontaneous Case Reports by Reporter



The Region of the Americas reported the highest count with 9,746,647 cases, followed by the European Region with 6,837,462 cases, the Western Pacific Region with 2,990,082 cases, the South-East Asia Region with 827,070 cases, the African Region with 263,037 cases, and the Eastern Mediterranean Region with 247,699 cases. Figure 2 illustrates the distribution of spontaneous case reports by reporter for each region individually. Percentage of the cases reported by the consumers (in the context of the total number of cases from this region) was assessed. The analysis revealed that the Region of the Americas exhibited the highest percentage of reports from consumers (with a ratio 2.29 times higher than the number of reports from physicians), whereas in all other regions, the number of reports from consumers was lower than the number of reports from physicians. The ratio of consumers to physicians' reports for other regions is presented in descending order: Eastern Mediterranean Region (ratio 0.87), European Region (ratio 0.70), African Region (0.38), Western Pacific Region (0.27) and South-East Asia Region (0.07). These results highlight a significant disparity in the reporting of adverse events by consumers across various regions.

The conclusion drawn is that, while the aggregate ratio of consumers' reports appears substantial, as illustrated in Figure 1, this is predominantly influenced by the high proportion of consumers' reports in the region of the Americas, while notably lower levels of consumers' reporting are observed in the African, Western Pacific, and particularly the South-East Asia Region. When interpreting this data, underreporting, a well-recognized limitation of spontaneous reporting systems, should be taken into consideration; it has been estimated that only 6% of all ADRs are reported.¹⁰ Additionally, it should be noted that underreporting displays significant variability across distinct regions.

Figure 2. Presentation of Spontaneous Cases by Reporter and Region of Origin

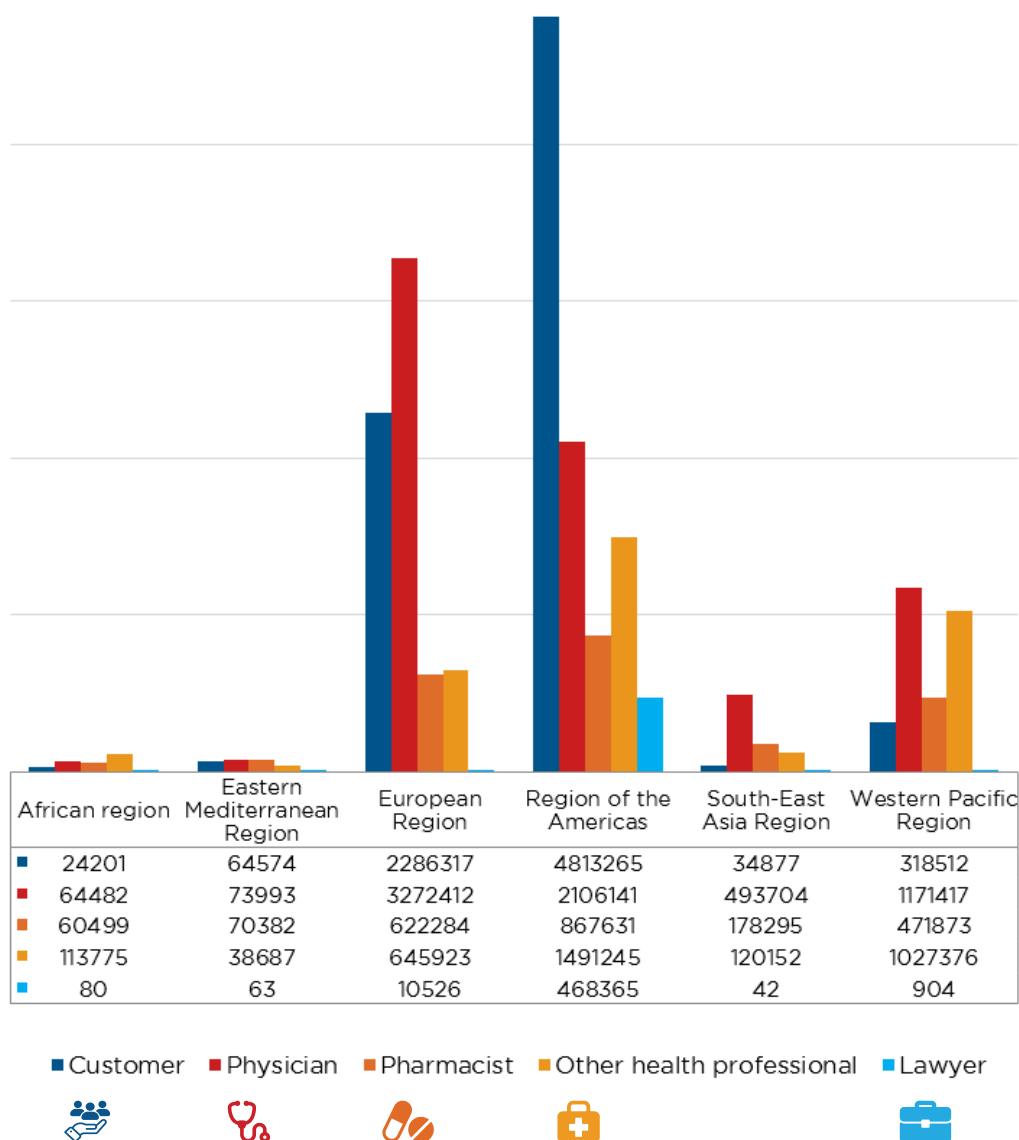
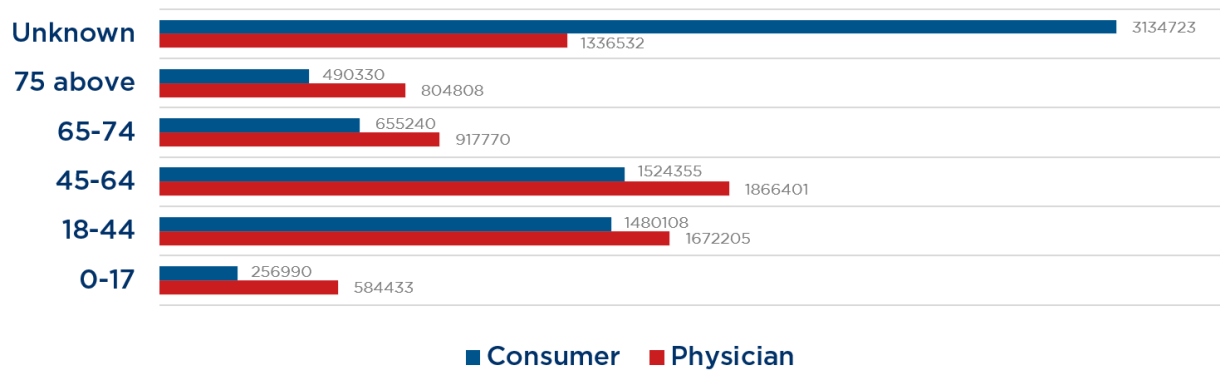


Figure 3 depicts the distribution of consumers' and physicians' reports across patients' age groups. Notably, the ratio remains consistently higher for physicians' reports across various age categories, except for cases where the age group information was unavailable. This outcome aligns with expectations, given that consumers' reports typically offer less comprehensive information, often resulting in the absence of patient age details.

Figure 3. Presentation of Spontaneous Cases Reported by Consumers and Physicians, Categorized by Age Group



The distribution of global serious case reports by reporter is showcased in Figure 4. Additionally, the separate distribution of serious case reports from the Region of the Americas by reporter is presented in Figure 5, acknowledging that this region constitutes the origin of the majority of the reports. The analysis reveals a global trend where physicians report a higher number of serious case reports compared to consumers (2,588,847 physicians' reports vs. 2,155,464 consumers' reports). Conversely, a contrasting pattern emerges for serious cases originating from the Region of the Americas, where consumers' reports surpass physicians' reports (1,442,962 consumers' reports vs. 810,311 physicians' reports).

Figure 4. Distribution of Global Spontaneous Serious Case Reports by Reporter

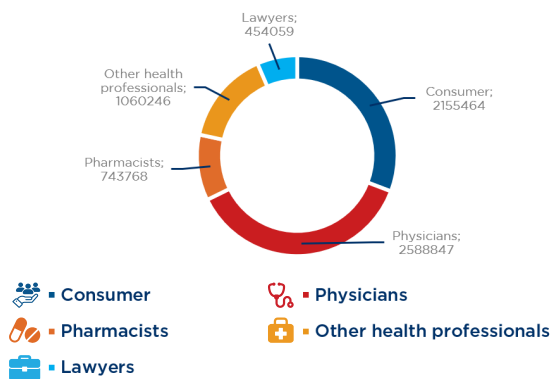
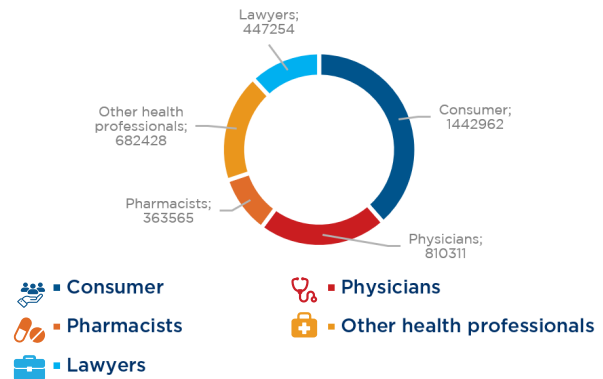


Figure 5. Distribution of Spontaneous Serious Case Reports from the Region of the Americas, by Reporter



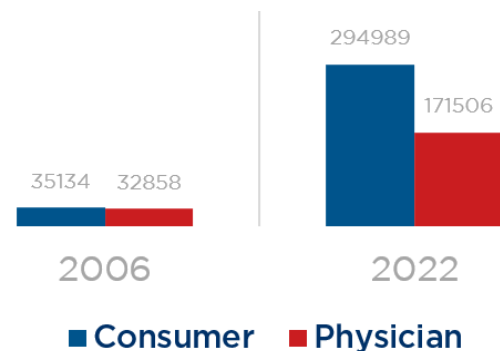
Considering that the highest number of spontaneous (consumer) reports in VigiBase derived from the Region of Americas, mostly from United States (US), FDA system was investigated for spontaneous reporting of adverse events and methods used to improve it.

In the Workshop regarding “The Roles of Consumers and Health-Care Professionals” from The National Academies Press, Washington, DC from 2007, workshop participants emphasized the need for increased consumer and advocate involvement in reporting events and ways in which this can be achieved¹¹. They concluded that public education programs that raise public awareness and communicate tangible public benefit of improved adverse reporting systems are ways in which patient advocacy groups and even patients themselves can play a role in reducing adverse drug events (ADEs). The development of an improved infrastructure for consumer reporting would also benefit from the increased input of those that the system was designed to serve. Engaging consumers to work with their health-care providers would be an important way to “connect the dots”. Consumer groups and patient advocacy organizations have begun to take steps toward providing consumers with consumer involvement in reporting adverse events. Consumers Union initiated the “Best Buy Drugs website” (www.crbestbuydrugs.org) to educate consumers about their medications. The website also provided information about diseases and disorders and common side effects for drugs in each class. The Internet has provided a very powerful tool for consumers to find and share information via e-mail lists, support groups, and networking. The Consumer Reports website (www.consumerreports.org) alone had more than 2 million active subscribers at that time. Initiative was to increase MedWatch visibility, to integrate reporting into the health-care delivery system, public service announcements and direct-to-consumer advertising, as well as distributing the form (and/or access information) to patients in relevant clinical care settings. Additionally, they recommended looking to successful reporting programs, such as the United Kingdom’s yellow card system which allows consumers to report online, by prepaid mail, and by phone.

Afterwards, in the US, the FDA has facilitated voluntary reports by consumers through several activities such as the release of a new consumer-friendly reporting form FDA3500B and the refurbishment of the interface of its online reporting system through the MedWatch program in 2013^{12, 13}. These efforts apparently have achieved an excellent outcome in enhancing voluntary reporting. The total number of voluntary reports in the US has increased, especially since 2013, and that consumers seem to have contributed to that increase. This was probably due to encouragement and increased public recognition that patients, could report AEs directly to the FDA, especially using the online reporting form¹⁴.

FDA official website today contains clear instructions for Consumers, guides, possibility for adverse events reporting online, via fax and phones. There are useful, simple ‘Minute for Consumers’ video instructions and ‘MedWatch Learn’ system to practice AEs reporting¹⁴. To assess the efficacy of the implemented measures in the Region of the Americas using the available VigiBase data, an additional comparison was performed. **Figure 6 illustrates the case reports documented by physicians and consumers in both 2006 and 2022.** Notably, a substantial increase in the total number of reports from patients and consumers was observed (67,992 in 2006 compared to 466,495 in 2022), along with an elevated ratio of consumers’ to physicians’ reports (1.07 in 2006 compared to 1.72 in 2022).

Figure 6. Case Reports Reported by Physicians and Consumers in 2006 and 2022



Conclusion

In summary, our study highlights the prominence of consumer reports originating from the Region of Americas, emphasizing regional disparities in patient engagement within spontaneous reporting systems. Drawing from the data collected from this region, it can be concluded that the implementation of an efficient reporting system, clear instructions and increased public awareness have demonstrated remarkable outcomes in enhancing patient participation in spontaneous reporting. These findings advocate for the adoption of these strategies as recommendations to amplify patient engagement in spontaneous reporting on a global scale.

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