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Key pharmacovigilance stakeholders' experiences of direct patient reporting of adverse drug reactions and their prospects of future development in the European Union

P. Inácio [a,*], A. Cavaco [b], E. Allan [c], M. Airaksinen [a]

[a] Clinical Pharmacy Group, Division of Pharmacology and Pharmacotherapy, Faculty of Pharmacy, University of Helsinki, Finland

[b] IMed.ULisboa Research Institute for Medicines and Pharmaceutical Sciences, Faculty of Pharmacy, University of Lisbon, Portugal

[c] Department of Pharmacy and Pharmacology, University of Bath, United Kingdom

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ABSTRACT

Objectives: In the European Union (EU), legislation allows patients to directly report adverse drug reactions (ADRs) to competent authorities. Five years after its implementation, patient reporting is not equal in all countries. This study aimed to explore key stakeholders' perceptions of patient reporting in four EU countries.

Study design: Qualitative study design.

Methods: Twelve representatives from national pharmacovigilance centres and/or authorities as well as national pharmaceutical industry bodies in four EU countries participated in the study. Supranational organizations were also included. Data collection was via face-semi-structured interviews. Inductive content analysis was performed thereafter, applying principles of risk management as a theoretical framework.

Results: Four themes (attitudes and beliefs, system maturation factors, regulatory improvements, and cultural shifts) emerged, conceptually interconnected. Participants from countries introducing patient reporting recently expressed a negative attitude. Participants highlighted the need for additional resources, both human and financial, to address patient reporting and associated advantages.

Conclusions: The findings identified perceived barriers and facilitators of patient reporting. The involvement of patients, use of information, and dissemination of patient reporting are far from optimal. A better integration of the work by EU regulatory authorities is recommended.

* *Corresponding author*. Clinical Pharmacy Group, Division of Pharmacology and Pharmacotherapy, Faculty of Pharmacy, Viikinkaari 5E Viikinakaari 5E – 7 Huone (P.O. Box 56), 00014 University of Helsinki, Finland.
E-mail address: pedro.inacio@helsinki.fi (P. Inácio).

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Introduction

Adverse drug reactions (ADRs) cause considerable mortality and morbidity, posing an important public health problem.[1] An estimated 3.6% of all hospital admissions are caused by ADRs, resulting in 197,000 deaths per year in the European Union (EU), at a cost of €79 billion.[2,3] Pharmacovigilance, 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 possible medicine-related problems, aims to optimize the safe use of medicine and improve patient care.[4] In the past few years, patients have been recognized as key contributors to pharmacovigilance.[5] This has been part of a wider trend to give patients a bigger saying in the management of their own health.[6] Patients have become important stakeholders in the process of drug regulation, providing important feedback on outcomes.[5] In the EU, patients' role has been acknowledged and expanded with the implementation of the EU pharmacovigilance legislation.[7] This legislation overhauled pharmacovigilance process across the EU and has put a bigger emphasis on the involvement of the general public.[8] It has also promoted greater transparency in the decision-making process and communication of outcomes.[9]

There is growing evidence that patients add value to pharmacovigilance through the spontaneous reporting system.[10] This method remains a core element of pharmacovigilance systems, despite its limitations.[11] Among them, underreporting is key, leading to false conclusions on the relative risk of medicines. The quality of information provided is also important, as poor quality reports do not provide sufficient details for an effective causality assessment.[12] Patient reporting was introduced as a way to complement healthcare professionals (HCPs) reporting in terms of quantity and quality thereby contributing to a more timely detection of signals of possible new ADRs.[13] A recent systematic review summarized patients' positive contribution as providing novel detailed information and contributing to safety signals. It also highlighted the importance of the qualitative information generated in helping to understand the real-file impact of ADRs.[10] However, there are concerns about the quality of the reports such as the identification of possible ADRs and its documentation, use of resources, awareness, or the origin of the reports.[13] Five years after the EU pharmacovigilance legislation implementation, patient reporting is increasing, with over 48,000 patient reports received within the EU in 2015 alone.[14] This new legislation changed the way medicines are monitored, but there are several questions concerning patient reporting. The European Medicines Agency (EMA) publicly recognizes patient involvement as valuable and necessary,[15] although little is known from organizations dealing with patient reporting on a daily basis.[16] Pharmacovigilance in the EU relies heavily on national competent authorities (NCAs). NCAs are the centre for implementation and enforcing, concentrate all the resources needed for these tasks, and are represented at the various committees of the EMA. Pharmaceutical industry complies with regulations laid down by the EU, interacting with authorities regarding risk management and postmarketing activities. They are legally obligated to report ADRs.[17] There is also important cooperation with international public health organizations. Before the implementation of the new EU pharmacovigilance legislation, patient reporting was already well established in countries such as the Netherlands, the UK, Denmark and Sweden.[7] Patient reports per million are highest for these countries.[7] For most of the remaining member-states, patient reporting was a new regulatory requirement with which they had little or no experience.[18] There are investigations into how member-states deal with patient reporting, as well as if regulatory requirements infringe on daily activities. More importantly, do different stakeholders acknowledge the contribution of patients to the system?

Considering the interdependency relations between the different stakeholders, the aim of the study was to explore reasons perceived by key stakeholders on the varying patient reporting of ADRs in four different EU countries. Focus was also put on exploring implications on the EU's system for safety monitoring of medicines' functioning.

Methods

Study design

A qualitative cross-sectional design with semi-structured interviews was used. An interview guide with 12 questions was developed and included as online Supplementary appendix (Online Resource 1). The interview guide questions were constructed based on the study aim, preparatory work and on a recent systematic review on the value of patient reporting.[10] The guide explored across the development of pharmacovigilance since the implementation of the EU pharmacovigilance legislation, with a special focus on the value of patient reporting. The interview guide was validated by members of the research team with experience in qualitative research (team members AC and MA), and revisions were made according to their input. The male researcher PI, pharmacist, conducted all the interviews. He had training in qualitative interviews before conducting them. For practical reasons, the guide was piloted with pharmacovigilance professionals in Portugal and Finland. After piloting the guide and aiming to capture as most detailed and complete data as possible, the guide was adapted but kept open to adjustments during data collection, particularly regarding different stakeholders' roles.

Sampling and recruitment

Pharmacovigilance in the EU comprises several stakeholders with a complex network of responsibilities. The organizations screened to be included in this study comprised NCAs or pharmacovigilance centres, on top of national pharmaceutical industry trade associations. In addition, supranational organizations were also included. These included the WHO, the Uppsala Monitoring Centre (UMC) and the European Federation of Pharmaceutical Industries and Associations. The organizations were chosen because of their involvement in implementing the EU regulations and processing patient reports (national authorities and pharmacovigilance centres); because of their regulatory compliance towards reporting ADRs (pharmaceutical industry trade bodies); and