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Overcoming Major Barriers to Build Efficient Decision Support Systems in Pharmacovigilance

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Abstract. Many decision support methods and systems in pharmacovigilance are built without explicitly addressing specific challenges that jeopardize their eventual success. We describe two sets of challenges and appropriate strategies to address them. The first are data-related challenges, which include using extensive multi-source data of poor quality, incomplete information integration, and inefficient data visualization. The second are user-related challenges, which encompass users' overall expectations and their engagement in developing automated solutions. Pharmacovigilance decision support systems will need to rely on advanced methods, such as natural language processing and validated mathematical models, to resolve data-related issues and provide properly contextualized data. However, sophisticated approaches will not provide a complete solution if end-users do not actively participate in their development, which will ensure tools that efficiently complement existing processes without creating unnecessary resistance. Our group has already tackled these issues and applied the proposed strategies in multiple projects.

Keywords. Pharmacovigilance, Decision Support Systems, Post-market Data

1. Introduction

The World Health Organization defines pharmacovigilance (PV) as the "science and activities relating to the detection, assessment, understanding, and prevention of adverse events or any drug-related problem" [1]. Regulatory agencies and other organizations worldwide maintain PV programs targeting efficient and rigorous detection of safety signals and subsequent evaluations for understanding unknown adverse reactions. Each program follows a specific process to ensure product safety objectives, but most of these processes involve manual steps that may jeopardize the successful completion of these objectives. Many organizations have recognized the inefficiencies and risks of manual processing and have sought to add automation to workflows by, e.g., classifying post-market reports [2] or delivering complete systems for safety review [3]. Unsurprisingly, these efforts focus more on software development than other critical barriers.

We strongly believe that other challenges must be addressed or, at least, adequately evaluated before initiating any software development and group them into two categories.

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First, there are challenges related to the adverse event data evaluated by safety reviewers and other experts, including data size, quality, integration, and visualization. Second, specific challenges are associated with the end-users of the PV systems, including overall expectations and engagement in developing automated solutions. This paper shares our multi-year experience in dealing with all these issues while constructing decision support tools and complete systems in PV. We extensively describe these challenges using specific examples and discuss ways to address them adequately.

2. Data-related Challenges in Pharmacovigilance

Safety reviewers analyze data from multiple sources to explore potential safety signals and confirm unknown new adverse drug reactions. In regulatory agencies, the starting point is the review of post-market reports submitted to spontaneous reporting systems, such as the Food and Drug Administration's (FDA) Adverse Event Reporting System (or FAERS). FAERS stores all post-market adverse event reports for drug products marketed in the United States and submitted by consumers, health care professionals, and other sources, usually through the manufacturers of these products. According to the FAERS public data, the number of annual submissions from 1968 to 2021 has increased exponentially (Figure 1). Safety review also requires evaluating other data sources, such as product labels, which further increases the amount of information to be analyzed and the workload for the human experts. As shown before, advanced methods, such as natural language processing, may efficiently support the review of big post-market data [4].

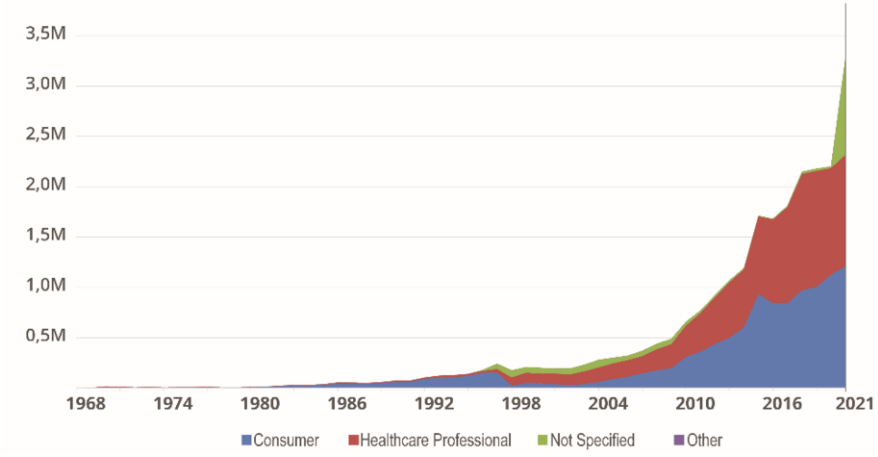

Figure 1. FAERS report counts (by reporter) from 1968, when FAERS was established, to the end of 2021.

Data quality is another barrier in PV. Spontaneous reporting systems like FAERS suffer from multiple quality issues, including incompleteness, inaccuracy, inconsistency, deduplication, and poor reporting [5]. The FAERS public release in Q3 2021 had missing values in key fields, e.g., age was missing in 40.3% of the cases. Imprecise information is often recorded as well, such as drug names that do not always adhere to the appropriate nomenclature. Another pair of issues is inconsistency and poor reporting when structured data do not match the corresponding values in the narrative and essential information,

such as temporal information, is either missing or partially reported. Last is duplication, when two or more reports describing an adverse event for the same patient are assigned different case numbers instead of being linked as the same case [6].

As mentioned above, safety reviewers must examine data from multiple sources other than the FAERS reports. A product label found in DailyMed contains all known adverse events discovered in the pre-market phase and identified in previous post-market reviews and serves as the baseline for recognizing potential new safety threats. Biomedical literature also contributes to a product's safety profile through new findings or evidence. The drug product is the entity that links all these sources, and given the widely known drug naming inconsistencies, data integration becomes challenging. In a recent implementation, we addressed this challenge by relying on FAERS data fields and Drugs@FDA to link FAERS, DailyMED, and PubMed information [7].

Data comprehension often comes best through visualizations; however, bar plots and pie charts (among the most commonly used visualizations) are usually inefficient, especially in the case of big data. Dense adverse event term listings or tiny pie slices do not help a reviewer easily and quickly understand a dataset (Figure 2). Data presentations must be compelling, efficient, and interactive. The bubble plot shown in Figure 2 is an excellent example as it conveys the same information about the frequency and outcomes of adverse events as the other two plots together.

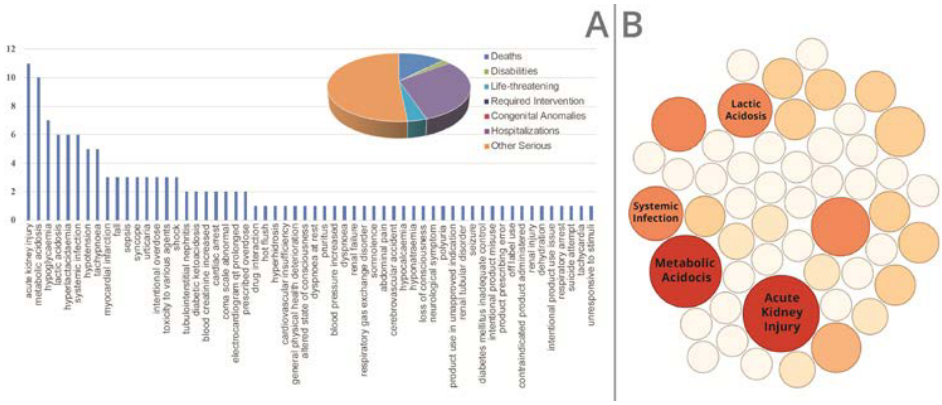

Figure 2. An alternative to overwhelming bar plots and inefficient pie charts (as in Panel A) might be a bubble plot (as in Panel B) that conveys the same information as the other two visualizations. Based on Q1 2019 FAERS public data.

3. User-related Challenges in Pharmacovigilance

The second set of challenges is related to end-user acceptance. It's not uncommon to see decision-support solutions fail to deliver on their objectives because end-users have not actively participated in the development cycle and evaluated the products extensively [8]. In most cases, either the developers consider this non-critical or end-users treat their involvement as an additional task without reward. Furthermore, automation creates resistance when viewed as bulldozing established workflows or forcing users to learn a new system that may not work well. Resistance will only grow when end-users have not been involved in the development and do not feel the system fulfills their needs. As a

natural reaction, they may raise their expectations, request an unachievable level of automated accuracy, and demand layers of quality assurance before accepting a new tool.

We can strike the right balance for all these challenges by following three routes. First, we can actively engage end-users in the development cycle with frequent meetings and feedback opportunities and coordinate with them to offer real evaluation scenarios. Second, we must fully understand existing processes and propose solutions that complement existing systems and processes rather than attempt to re-write them. Third, prioritizing the automation of individual time-consuming tasks may immediately solve major issues and create more trust for complete systems.

4. Discussion

This paper has described a generalized set of challenges faced while developing decision support tools for PV, including data-related and user-related issues. However, none of these issues are insurmountable, and real progress in system development can be made with suitable approaches. A software solution for PV needs to integrate and contextualize data (sometimes poor quality) from multiple sources and present it effectively and efficiently to facilitate specific user workflows. This development requires close collaboration with end-users to target their concerns on large- and small-scale issues.

We believe these challenges and mitigation strategies are applicable across the field of PV and encourage all organizations and developers working on decision support designs to consider how they can address them at the beginning of their work rather than at the end. Undoubtedly, such approaches are time-consuming and require parallel management of complex processes. The team in charge must also overcome organizational, implementation, and other barriers to deliver a system within a particular timeframe using limited resources. “Getting the job done” will satisfy the contract terms but will not necessarily solve any problems. We argue that putting all challenges on the table, inviting all stakeholders to share their perspectives, and making a solid plan is likely the right place to start before reaching out to the developers.

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