Unlocking Real-World Evidence in post marketing surveillance: The Critical Role of Scientific Management

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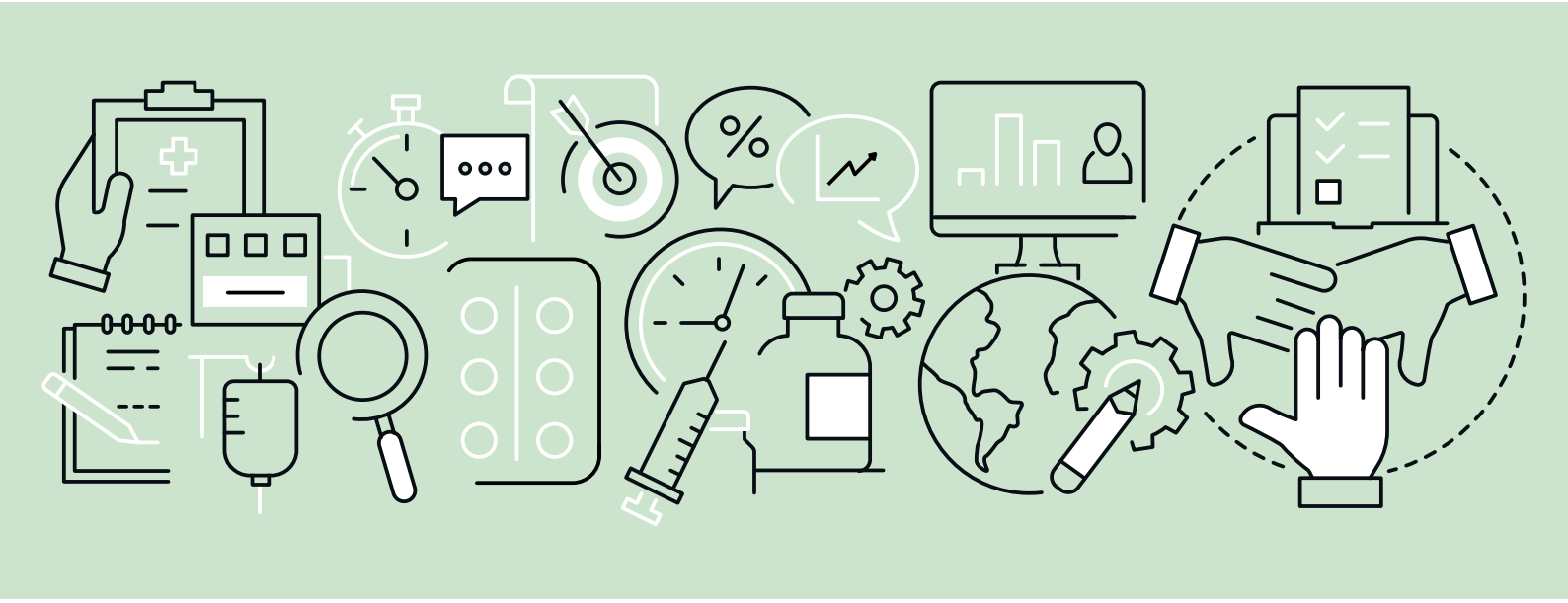

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Content

Introduction

The use of real-world evidence (RWE) has brought a significant change in the monitoring of medicinal products safety and effectiveness after they receive marketing authorisation.[1,2]

By combining and analysing harmonised data from multiple sources, collaborative multi-database studies (MDS) can generate real-world evidence (RWE) that demonstrates how medicinal products perform across various patient groups in real-world settings, providing a more comprehensive view of their safety and effectiveness profiles.[3,4] However, these types of studies require active involvement of multiple stakeholders as well as collaboration across different disciplines and expertise to ensure the robustness and reliability of the generated evidence. Furthermore, coherence with evolving regulatory requirements is crucial to guarantee the validity and acceptance of RWE findings.

In this dynamic landscape, the role of scientific managers has become increasingly important. They facilitate interdisciplinary collaboration while providing guidance in navigating the complexities of MDS for the generation of RWE in post-marketing surveillance of medicines. Scientific managers play a pivotal role in orchestrating collaborative research, fostering synergies across diverse stakeholders, and ensuring the smooth and effective execution of the different stages of the studies.

In this white paper, we explore the role and skills required by scientific managers in the life-cycle of post-marketing authorisation safety and effectiveness studies.

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RWE in post-marketing surveillance

After the thalidomide crisis in the 1960s, post-marketing surveillance of medicinal products has progressed rapidly. Since then, the use of RWE derived from electronic health records (EHRs), claims databases, patient registries, and other real-world sources has been highly valuable to identify, confirm, and assess potential safety signals of marketed medical products.[5] In 2018-2019, the European Medicines Agency (EMA) reported that approximately 40% of the Marketing Authorisation Applications (MAAs) submitted to the agency incorporated RWE. The main use of RWE in these applications was for post-authorisation studies, representing 68.3% of MAAs. This inclusion of RWE was mostly driven by the regulatory agency's requirement (specifically under category 3 of the risk management plan) to support evidence of safety and efficacy.[6]

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The significance of real-world data (RWD) in informing public health policies and assessing the safety and efficacy of treatments and vaccines became evident during the COVID-19 pandemic.[7] As a result, regulatory bodies around the world introduced various measures, such as guidelines for RWE studies, which they keep updating, whilst developing new ones to encourage the widespread use of RWD throughout the different stages of a medicinal product's life-cycle.[8,9] In this context, the use of a federated approach to RWE generation involves the harmonisation and analysis of data from multiple sources without centralising it. This federated strategy allows data to remain within its original setting, such as individual healthcare institutions or databases, while still allowing collaborative analysis across these distributed sources. There are several benefits to working with federated networks:

1) researchers can gain insights without compromising data privacy or security,[10]
2) higher statistical power and variability of population enable large cohort analysis across healthcare institutions, regional, and national borders,[10,11]
3) use of common infrastructure with harmonised interoperability standards and tools significantly improve replicability, increase transparency, and reduce bias.[12]

The success of MDS for post-marketing surveillance of medicines relies on the effective collaboration and the synergistic contributions of diverse experts such as pharmacoepidemiologists, biostatisticians, programmers, medical writers, data managers, clinicians, pharmacists, and scientific managers. Each stakeholder plays a crucial part in ensuring the generation of high-quality, reliable RWE to inform healthcare decisions and contribute to patient safety.

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The role of scientific managers in post-marketing RWE studies

The importance of research support staff is increasing in research institutions and initiatives.[13] Scientific managers combine a strong scientific background with expertise in management to actively contribute to the implementation of research projects. Their pivotal contributions in translating scientific goals into actionable project blueprints, devising innovative and effective solutions to complex challenges, and turning findings into impactful publications, collectively contribute to the greater efficiency and speed of research and its outcomes.

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In pharmacoepidemiology research, the scientific manager is crucial for addressing the challenges inherent to collaborative RWE studies.

Scientific study managers are involved in all phases of the study, from the initial outline and protocol development to the study's closure. They undertake various duties during study execution to facilitate decision-making processes and ensure the overall quality of the studies.[14] Scientific managers' most frequent responsibilities relate to study planning and monitoring and include facilitating meetings and discussions, negotiating with study partners, finding key experts for specific tasks, tracking timelines and outcomes, checking study documents for quality, and setting criteria for their assessment.

Beyond these operational aspects, scientific managers also have a significant role in **shaping and enhancing the technical aspects of the studies**, thus conferring a tangible structure to research ideas and actions. This includes active involvement in study implementation and reporting, achieved through continuous monitoring in collaboration with the study scientific coordinator or principal investigator, ensuring the quality and integrity of the data from diverse sources, and helping to navigate the complicated regulatory landscape that governs post-marketing surveillance studies. Importantly, thanks to the comprehensive understanding of the entire study, the scientific manager is well-placed to **identify risks and study bottlenecks**, which are then communicated to the scientific lead for appropriate analyses and counteractions.

Planning and Monitoring	• *Effective multi-stakeholder communication* • *Negotiation with study partners* • *Task assignment according to expertise* • *Quality criteria and checks of study documents* • *Overall study integrity*
Technical implementation	• *Data monitoring, management, interpretation, and analysis* • *Reporting* • *Regulatory compliance*
Risk Management	• *Identification of potential risks and study bottlenecks* • *Support scientific lead in risk analysis and development of mitigation and contingency plans*

Table 1: Frequent tasks perfomed by scientific study managers

Due to the interdisciplinary nature of their role, scientific managers have experienced an increasing demand to **intensify their involvement in research and take on a broader scope of tasks**. Despite their significant contributions, the role of the scientific manager is not always appropriately recognised, reflecting the challenges faced by other research-supporting professions, as highlighted in the ARMA Research Culture Survey Report.[15] Calls for cultural change to acknowledge the roles of non-academic staff have been echoed in position papers.[16] Even widely accepted models such as CrediT (Contributor Roles Taxonomy), adopted by most scientific publishers, acknowledge project administration and management as major contributions to research outputs.[17]

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COVID-19 as a game-changer: lessons learned from the pandemic

Effective management of uncertainty, adaptation to fast-changing regulations, adoption of quality management practices, fostering stakeholder collaboration, embracing change management, and process optimisation through the use of appropriate tools and quality criteria, flexibility, and prioritisation have been identified as crucial factors for the successful coordination of MDS during the pandemic. However, **the COVID-19 era also poses regulatory and conceptual challenges that have a lasting impact on pharmacoepidemiology studies**. The shorter timelines and innovative methodological frameworks adopted during the pandemic have altered the research landscape in this field. COVID-19 has changed the rules of the game and there is no turning back.

Developing skills for effective scientific management

The vital role and impact of scientific managers in pharmacovigilance research highlights the importance of developing both soft and hard skills for their success (Table 1). Soft skills, such as **effective communication, leadership, problem-solving, and teamwork, are essential for building constructive collaborations** with diverse stakeholders, such as researchers, data analysts, regulatory authorities, and health-care professionals. These skills enable study managers to navigate complex interpersonal dynamics, overcome communication barriers, and create a positive work environment, thereby enhancing research outcomes. On the other hand, mastering hard skills, such as **data management, research methodology, statistical analysis, and regulatory science, empowers scientific managers to handle the technical aspects of multi-country RWE studies** with competence, thus creating an efficient and well-structured research environment.

A deep understanding of the research process, including data collection, harmonisation processes, analysis methods, and data storage requirements, are important for ensuring the accuracy and reliability of the study's findings. Moreover, given the evolving landscape of research regulations, study managers must keep up to date with the latest guidelines and requirements to **support smooth regulatory decision-making processes**.

Soft Skills	Hard Skills
EFFECTIVE COMMUNICATION	SCIENTIFIC AND REGULATORY KNOWLEDGE
TEAMWORK	PROJECT MANAGEMENT
CHANGE MANAGEMENT	RISK MANAGEMENT
CONFLICT MANAGEMENT	DATA MANAGEMENT
INNOVATIVE THINKING	QUALITY ASSURANCE
PROCESS OPTIMISATION	DOCUMENT MANAGEMENT
	LEGAL AND FINANCIAL MANAGEMENT

Table 2: RWE Study Managers Skills

Due to the highly specialised nature of the role, in some studies a team of study managers with different expertise may be needed in order to cover all the skills required.

Next, are key considerations for developing study manager key skills.

Soft Skills

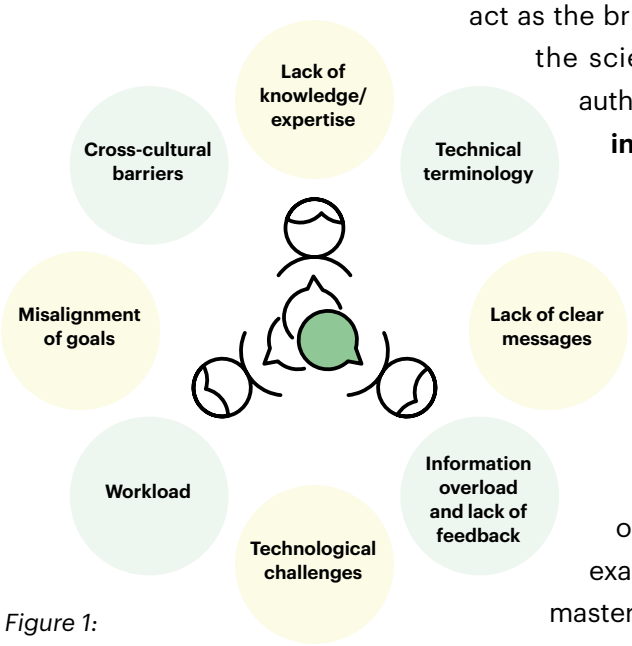

Figure 1: Communication barriers examples

COMMUNICATION

Effective communication is crucial for scientific managers as they act as the bridge between various stakeholders, including the scientific lead, study partners, and regulatory authorities. They should be able to **convey complex information clearly** and efficiently, ensuring that everyone is on the same page and understands their roles and responsibilities. Some of the barriers that may influence the group communication, resulting into potential study delays are described in Figure 1. The study manager should be able to identify them and act accordingly. Additionally, effective communication is important when reaching out to a broad audience or engaging patients, for example in webinars or conferences. In this context, mastering the use of plain language is essential.

TEAMWORK

Successful multi-country studies require **effective collaboration** with various partners, including healthcare institutions, researchers, and regulatory authorities. Scientific managers should have the skills to **create and sustain solid working relationships** with stakeholders, **keeping study teams driven and aligned**, and encourage a collaborative spirit throughout.

CHANGE MANAGEMENT

The ability to navigate and **adjust to fast-changing requirements and circumstances** is essential. Scientific managers should anticipate potential obstacles and apply strategies to manage change effectively, **ensuring minimal disruptions to the study's progress**.

CONFLICT RESOLUTION

Conflicts may arise due to the complexity of multi-country studies and diversity of partners involved. A scientific manager should have strong conflict resolution skills to **address and resolve issues promptly**, fostering a collaborative and harmonious work environment.

INNOVATIVE THINKING

The ability to think outside the box and find innovative solutions to challenges is invaluable. Study managers should be **flexible and resourceful in devising strategies** to overcome obstacles.

PROCESS OPTIMISATION

Striving for continuous improvement is vital to enhance the efficiency and effectiveness of the study. Study managers should be proactive in **identifying areas for improvement** and implementing **measures to optimise study processes**.

Hard and Technical Skills

SCIENTIFIC AND REGULATORY KNOWLEDGE

Study managers must have a solid understanding of the scientific and regulatory landscape, especially in the context of pharmacovigilance and real-world data research. **Keeping up with the latest regulations and guidelines is crucial**, as regulatory requirements are continuously evolving.

PROJECT MANAGEMENT

Strong project management skills are fundamental to ensure the smooth initiation, execution, and completion of the study. Study managers should be well-versed in **planning, organising, and monitoring project timelines, deliverables, and documentation.**

RISK MANAGEMENT

During the course of a study, multiple risks may arise. Study managers should be able to **identify, assess and prevent or mitigate risks** during the study period that may have a potential impact on the outcomes. Risk assessment tools can be used to measure risk levels considering their impact and probability to occur.

DATA MANAGEMENT

As studies involve large healthcare data sources, study managers should have skills in data management and analysis. Familiarity with **data collection methods, database systems, and statistical analysis** will aid in deriving meaningful insights from the collected data.

QUALITY ASSURANCE

Maintaining high-quality standards throughout the study is essential for regulatory decision-making. Scientific managers need to stay updated with regulatory requirements and be **competent in performing quality control, audits, and assessments**, to ensure compliance with quality standards.

DOCUMENT MANAGEMENT

The conduction of pharmacoepidemiology studies entails managing large and complex documents, from **protocols and statistical analysis plans to study reports and manuscripts**. The scientific manager, in collaboration with the study investigators and medical writers, must have the skills to oversee and contribute to the **writing, editing, regulatory compliance, content clarity, and versioning control** of the documents.

LEGAL AND FINANCIAL MANAGEMENT

The proper initiation and progress of studies involving multiple partners rely on crucial legal and financial aspects. Therefore, scientific managers should be capable of **engaging in discussions with legal professionals** regarding contracts, and other agreements, particularly those regarding data protection issues. Additionally, they should be **proficient at budget calculations**, including discussions about budget reallocations based on specific needs.

Conclusions

The use of real-world evidence in collaborative MDS has revolutionised the monitoring of medicines after marketing authorisation and will play an increasingly important role throughout the entire life cycle of drug development. In this transformative landscape, scientific managers play a central role in navigating the complexities associated with MDS. By fostering collaboration, ensuring regulatory compliance, and orchestrating the efforts of diverse stakeholders, scientific managers contribute significantly to the generation of reliable and meaningful RWE for the post-marketing surveillance of medicines. This extensive skill set enables them to address the challenges posed by the dynamic research environment, particularly when conducting multi-country RWE studies for regulatory decision-making during and after the COVID-19 pandemic.

As the importance of the scientific manager's role is increasingly recognised, the focus on developing these competencies will underscore their contribution in advancing scientific knowledge and achieving impactful research outcomes. Investing in their professional development not only benefits individual study managers but also strengthens the research ecosystem, fostering a culture of excellence, collaboration, and innovation.

As the importance of the scientific manager's role is increasingly recognised, the focus on developing these competencies will underscore their contribution in advancing scientific knowledge and achieving impactful research outcomes

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