Better Decision-Making for Better Outcomes:

a Call to Action on Harnessing the Power of Real-World Evidence

Recent years have seen growing recognition of the role that data can play in enabling not only better health system performance, but also better health experiences and outcomes for patients – "outcomes that matter." Real-world data (RWD), in particular, (i.e. routinely collected data relating to patient health status or the delivery of health care from a variety of sources other than traditional clinical trials[1]) is increasingly recognised as a critical means through which to improve public health, as is the real-world evidence (RWE) that is derived from analysis of RWD.

Challenges

In 2022 the International Coalition for Medicine Regulatory Authorities[2] acknowledged the importance of RWE by calling for international collaboration to integrate data from real-world sources into regulatory decision-making. There are challenges that must be addressed, however, especially with regard to national regulatory authorities' varying – and in some cases restrictive – approaches to considering RWE, the lack of standardised RWE definitions and divergence in the ways that RWD is collected not only across countries, but also within national healthcare systems.

Case studies illustrating the importance of RWE for effective health decision-making

Real-world evidence complements randomised clinical trial (RCT) data by enabling a holistic understanding of the effectiveness of medicines (including vaccines), their impact and their safety. It enables this understanding for large, heterogeneous populations as well as small rare disease communities. It plays a crucial role in enabling better health outcomes for patients as well as creating economic value[3] and, therefore, enhances decision-making effectiveness while bolstering health system sustainability.

Influenza, rare diseases, and cancer are three disease areas which illustrate the fundamental role that RWE does or should play in informing scientific understanding, health policies and decision-making:

1. As defined by the European Medicines Agency
2. See ICMRA statement on international collaboration to enable real-world evidence for regulatory decision-making (2022)
3. As stressed by the Proposal for a Union regulation on the European Health Data Space (2022, p.14)

INFLUENZA

- Vaccines confer protection against seasonal influenza, especially for those most at risk of developing severe disease, such as older adults and people with chronic conditions. RWE is particularly important for influenza vaccines due to the variability of influenza seasons, occasional mismatch between circulating virus strains and those that the vaccines target, and the difficulty of generalising findings from one or two seasons. The circulating strains and four strains that are in each year's seasonal influenza vaccine change so often that a longitudinal view of vaccine performance is essential.

- In light of the above, it would not be feasible or useful to run multiyear RCTs with each year's seasonal influenza vaccine. RWE of various kinds that is acquired through observational studies – which accounts for the vast majority of available data on the vaccines – is therefore crucial to understanding the effectiveness, impact and safety of vaccines.

- RCTs are considered "gold standard" data for regulatory purposes but represent a small subset of the available data on influenza vaccines. A holistic understanding of the effectiveness, impact and safety of influenza vaccines thus requires a balanced approach to considering the full evidence base of RCTs and RWE and recognising the strengths and weaknesses of the associated data.

RARE DISEASES

- In the field of rare diseases, small patient populations with high unmet needs make recruitment into RCTs a challenge. Moreover, it can be difficult to identify control groups, with the added challenge that, in the case of life-threatening conditions, the use of control groups would also be considered unethical.

- RWE, including the development of registries, can provide a comprehensive understanding of the patient population for rare diseases, including those who may not be well represented in clinical trials, and provide insight into the impact of the disease on patient quality of life.

- Furthermore, RWE can provide data to support the development of clinical guidelines and inform reimbursement decisions, which can be particularly important in the context of rare diseases, where funding is often limited, and outcome-based agreements using RWE may provide solutions to help governments manage budget impacts while appropriately rewarding critical, transformative and innovative therapies.

ONCOLOGY

- Recruitment of patients into RCTs is highly selective, leading to the exclusion or under-representation of certain sectors of the relevant population. As with rare diseases, some types of cancer (e.g., paediatric cancers or other rare cancers) may have limited patient numbers, making data generation in the context of an RCT very challenging.

- A particular benefit of RWE is the possibility to gain insights into patient sub-populations, or patients living in different geographical locations, which may not be represented in RCTs.

- Additionally, RWE gives a more complete picture of the medicine used in realistic situations, including incorrect treatment administration or missed doses. Alongside RCTs, RWE can provide insights into real-world treatment patterns, outcomes and populations and thereby inform future RCT designs, treatment guidelines and policy decisions.

POLICY ASKS

Systematic use of RWE can deepen understanding of medicines (including vaccines), enhance policy decisions and facilitate the access of EU citizens to effective medicines. We call on policy makers, regulators and payers to:

1 Ensure that RWE is appropriately taken into consideration when approving and assessing medicines and creating policies that will guide their use, ensuring that decisions are based on an appropriately holistic understanding of the effectiveness, impact and safety of medicines.

- Ensure that decision-making gives appropriate weighting to RWE from physician- and patient-reported outcomes, including studies with and without confirmation of laboratory results where appropriate, to ensure a comprehensive evidence-based evaluation.

2 Enhance access to RWE for decision-making and scientific research purposes.

- Reinforce the use of RWE and patient-reported outcomes in the design of clinical trials, to improve the richness and reliability of datasets when population sizes are reduced, especially when tackling rare and ultra-rare diseases.
- Clarify responsibilities and support the active engagement of the patient and medical communities in RWE generation.
- Facilitate the use of RWE generated after the launch of a treatment to increase the understanding of its benefits, the evolution of unmet medical needs, and tackle challenges in evidence collection.
- Adapt the design of RWE to specific treatments while also supporting the utility of registry data in regulatory decision-making, ultimately resulting in an enhanced patient experience.

3 Support the standardisation of definitions of RWD and RWE to improve data collection and enable an improvement in the overall consistency and quality of data.

- Ensure that RWE registries and reports are interoperable across the EU.

4 Promote best practice exchange and ongoing interactions between government bodies, academia, civil society and industry for enhanced collaboration in the production of RWE and the exploration of scientifically sound, pragmatic approaches through which RWE can inform policymaking.

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