Harnessing the patient voice in real-world evidence: the essential role of patient-reported outcomes

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Real-world evidence is increasingly valued by regulators and payers. Central to this evidence base is patient-reported outcome data describing the impact of drugs on quality of life, daily activities and symptoms. Here, we highlight key challenges with current real-world, patient-reported outcome data and describe collaborative next steps for international stakeholders to overcome these issues.

Data sources for real-world evidence include electronic health records, insurance claims and billing, registries or on-site medical chart review. However, information about how patients feel and function, as captured directly from patients themselves, is often missing[1]. As pressures from legislation, international regulatory authorities and patient groups promote more patient-centric drug development and evidence generation[2], attention is now turning to the role of patient-reported outcomes (PROs) to provide the patient perspective in real-world data sets.

By definition, PROs represent health status as reported directly by the patient, without interpretation by a clinician or anyone else[2]. PROs are collected via questionnaires that elicit information about symptoms, physical functioning and/or health-related quality of life. Here, we first overview the challenges in collecting, analysing and integrating PRO data with other forms of real-world evidence, and then put forward strategic priorities to help address these challenges.

Current challenges in PRO real-world evidence

Advances in health informatics infrastructure and capabilities for analysing complex large data sets bring opportunities to better characterize the experiences of patients during typical care. Historically, most PRO collection has occurred in prospective randomized clinical trials, to inform regulatory decision-making, health technology assessment, reimbursement and clinical practice guidelines. However, in real-world contexts, prospective PRO collection has been limited and fragmented to date, with PROs collected in only 14% (8 out of 57) of recent post-authorization safety studies, consisting largely of one-off registries for post-marketing assessment sponsored by drug manufacturers in specific populations[1]. Furthermore, secondary sources of real-world data such as electronic health records and insurance claims often do not capture PROs. Even in rare cases when PRO data are collected as a part of routine care delivery, PRO objectives are often not clearly defined, the items collected are not consistent across the same patient group in different regions and the terminologies and timings of assessments are not standardized. This may hinder the integration and interpretation with other data sources, resulting in a missed opportunity for learning more about therapeutic interventions and the overall patient experience[3].

Mandated approaches to PRO collection for audit and benchmarking purposes, such as the UK PROMs initiative (see Related links), have been an important first step in attempting to assess patient-centred health gain within the National Health Service in the UK. However, to ensure full integration of PROs, there is a need to improve the efficiency of the data collection, develop guidance on how best to interpret and utilize the data and gain 'buy in' from clinicians and patients regarding the added value[4]. PRO data collected in a real-world setting needs to generate benefits for patients and clinicians for broader benefits to be fully realized[3].

Vision and strategic priorities

Our vision is to ensure high-quality, systematic collection of real-world PRO data that can meaningfully inform patient-centred drug development throughout the product life cycle. The opportunity to benefit patients, health-care professionals and society is substantial. In early phases of development, real-world PRO data can provide evidence of the burden and natural history of disease, supporting the selection of the most appropriate primary and secondary end points for trials. PROs in early access and compassionate use schemes can provide additional complementary insights to the clinical trial data before drug licensing and help protect patient safety with PRO alerts. Once

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a drug has been licensed, PROs can provide data on long-term tolerability, safety and effectiveness in populations that are more representative than pre-approval trials, affecting clinical decision-making and guideline development, and supporting managed access programmes. For example, for novel drugs, such as advanced therapies, with high up-front costs but long-term treatment effects, demonstration of the lifetime effects of therapy will play an important role in reimbursement. Real-world PRO data can also provide benefits at the individual patient level by enabling real-time symptom monitoring and tailoring of care to individual patient needs[3].

Some key considerations in the design and implementation of PRO programmes for real-world evidence generation, derived from standard approaches in more established research contexts such as prospective clinical trials and cohort studies, are summarized in Supplementary Table 1. Implementation can be resource-intensive, and so institutional and ground-level support for integration into workflow and technology infrastructure and consideration of who pays for data collection are essential components for success. To optimize PROs, we consider the following to be key strategic priorities.

- Ensure international collaboration across multiple stakeholders including patients, caregivers, clinicians, regulators, ethicists, industry, payers and policy makers to agree to a standardized approach to PRO assessment.
- Develop a comprehensive standard set of recommendations, methods and tools that are applicable to generation of real-world evidence based on PROs in different settings. Such recommendations should be applicable to both primary data collection in prospective registries and secondary data from electronic health-care records.
- Formulate a clear governance process for generation of real-world evidence based on PROs, including an ethical framework for how patients should be consented (including implied consent in clinical forms completed by patients), who selects patients, who can access data and how data will be used[3].
- Establish standard sets of PRO measures, electronic tools and administration schedules to raise the bar. In this respect, there are ongoing efforts (for example, the FDA exploring a common PRO assessment strategy and the European Union Innovative Medicines Initiative (IMI) GetReal project).
- Develop and use electronic PROs wherever possible.
- Minimize workload and technical complexity for patients, clinicians and health providers.
- Carefully consider the objectives of PRO assessment, the timing of assessments, length of follow-up, minimization of missing data and inclusion of patients from diverse backgrounds[5].
- Ensure data collection adheres to the FAIR (findable, accessible, interoperable and reusable) guiding principles for scientific data management and stewardship.
- Provide guidance on how to interpret and use the data.
- Ensure patients and clinicians gain value from assessment through real-time access to PRO data to tailor care to individual needs[3].

Conclusion

In summary, PROs represent health status as reported directly by the patient and offer the potential to capture how a patient feels and functions during routine care, providing information that is useful to the patient themselves with regard to treatment choices, to the health-care professional and to the health service provider. Without PRO data, real-world evidence will not actually reflect how real patients experience real therapies in the real world. And for these data to be useful, the standardization of methods for PRO collection, analysis, and reporting is essential, as is the availability of standard PRO data collection tools.

We have highlighted a number of key considerations in the design and implementation of PRO programmes for real-world evidence generation. Incorporation of real-world evidence in regulatory decisions, clinical practice guidelines and health policy is still nascent. But as momentum increases and aggregated clinical data become increasingly available for real-world evidence, attention should turn to increasing international collaboration, developing the required tool kit and consistently complementing these real-world data with PROs.

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Competing interests

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Supplementary information

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