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SYSTEMS CHANGE

Key challenges for patient registries – A report from the 1st workshop of the EHC Think Tank Workstream on Registries

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Introduction: Patient registries are an invaluable resource for furthering the understanding of rare diseases such as bleeding disorders, providing large, pooled datasets not achievable by other means of data collection. As well as supporting clinical care and research, registries must also be able to answer questions that are important to the wider bleeding disorders community. However, there are challenges associated with the need for secure access, exchange of health data, quality and interoperability, and data delivery. **Identifying key challenges:** As part of the EHC Think Tank Patient Registries Workstream, 17 stakeholders representing health care providers, patient groups, research and industry met in October 2021 to identify challenges to managing and utilising patient registries, from each of their stakeholder perspectives. This is a first step in a longer term process aiming to identify or co-create solutions that could improve access and interpretation of patient data. The challenges identified relate to five key categories which are interlinked in various ways: 1. The multiplicity of registries and datasets; 2. Data quality; 3. Data sharing; 4. Expanding the scope of registries; 5. The role of the patient in registries. **Summary:** The heterogeneity in the way that registries are designed, funded and owned, the type of data collected, and the way data is collected are issues that must be addressed. Good, quality data is needed at all levels to ensure the provision and funding of effective care. Data quality will increase overall if it is possible to merge data from different registries. The value of patient participation in registries must also be acknowledged and built on to help ensure their quality, that they remain fit for purpose, and that data input is sustained over time.

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As tools that aid the understanding of bleeding disorders and the individuals who live with them, patient registries make a vital contribution to the development of care. In an age of novel technologies, it is essential that they are able to support research, assessment and safety monitoring in the longer term.

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Patient registries are an invaluable resource for furthering the understanding of rare diseases. They provide large, pooled datasets that are not achievable by other means of data collection, and many have the potential for record linkage. However, they are not without challenges, as highlighted by the European Health Data Space (EHDS) initiative [1]. This European Commission priority initiative aims to drive the transformation of health care across Europe. It identified strong data governance will be needed for the secure access and exchange of health data, the pooling of health data to promote research and personalised health care will require data quality and interoperability standards, and infrastructure and technological input will be essential in delivering data and digital tools [2].

As in many other rare conditions, registries relevant to bleeding disorders care exist at international, national and regional level. They may be specific to a range of bleeding disorders, specific bleeding disorders, or rare diseases more broadly [3]. Used by multiple stakeholders, the data they hold support and are used in various ways in clinical care, research, epidemiology and pharmacovigilance [4]. Importantly, they can provide insights into the needs, and in some cases financing, of people with bleeding disorders.

However, history suggests that registries have been slow to answer questions of importance to the wider community, for instance around the epidemiology of inhibitors in those with haemophilia. Ahead of the introduction of novel technologies, the EHC Think Tank wishes to address these issues, focusing both on the need to gather better data to understand the whole patient group and different types of treatment. This will help to ensure that future health technology assessments and research are able to call upon more and better data, and that long-term safety monitoring of novel technologies will be as robust as possible.

IDENTIFYING KEY CHALLENGES

In the first session of the EHC Think Tank Workstream on Patient Registries in October 2021, 17 stakeholders representing health care providers, patient groups, research and industry participated in a virtual meeting to identify challenges to managing and utilising patient registries, and to propose potential solutions that could improve access and interpretation of patient data. As part of this meeting, participants were split into four 'breakout' groups to consider in depth the key challenges facing patient registries and their users. Each group was tasked with identifying up to four challenges based on a template where they identified which stakeholders were affected by that particular challenge and why, and which stakeholders may hold a solution to that challenge and why (Figure 1). The breakout group results were subsequently fed back to and discussed among all workstream participants.

The challenges identified were grouped into five categories:

- Multiplicity of registries/datasets
- Data quality
- Data sharing
- Expanding the scope of registries
- The role of the patient in registries

These challenges are interlinked in various ways, as is shown below.

BLEEDING DISORDER REGISTRIES

A number of registries have been developed to serve the haemophilia community. These include the Pediatric Network on haemophilia management (PedNet, *https://pednet.eu*), the World Federation of Hemophilia World Bleeding Disorders Registry (*https://www.wfh.org/en/our-work-research-data/world-bleeding-disorders-registry*), and the European Haeomphilia Society Safety Surveillance registry of adverse events (EUHASS, *http://web.euhass.org*).

There are also many national agencies that maintain registries, including the Banque Nationale de Données Maladies Rares (*https://www.bndmr.fr*), the UK Haemophilia Centres Doctors' Organisation (UKHCDO, *http://www.ukhcdo.org*) and the Swiss Rare Disease Registry (*https://www.ispm.unibe.ch/research/research_groups/child_and_adolescent_health/paediatric_and_rare_disease_registries_and_other_studies*). Spain has many examples of regional registries – among others, in the Basque country, Catalonia, Murcia and Galicia.

A comprehensive list of registries worldwide is available from Orphanet at *https://www.orpha.net/consor/cgi-bin/ResearchTrials_RegistriesMaterials.php*.

1. MULTIPLICITY OF REGISTRIES/DATASETS

If registries are to fulfil their potential to improve patient care, the collection and utilisation of the data they hold must be efficient and accessible. The number

Figure 1. Template for identifying challenges for patient registries

Challenge:

For whom is this a challenge?

Why is it a challenge for them?

Who might hold a key to a solution?

Why?

and diversity of patient registries and the datasets they contain often exist in isolation ('data silos') and in formats that are not fully compatible, meaning their data cannot easily be integrated. Even within a single country, inter-regional differences in health care provision can mean that registries for the same group of patients are incompatible.

This multiplicity of registries poses a challenge for all stakeholders – those who submit data, people working in different professional areas with their own data standards, organisations and individuals in different countries who need to carry out research, and regulators trying to deliver effective data protection. Ultimately, this challenge impacts on the patients who could benefit from what might be learned by combining datasets.

The existence of multiple registries with overlapping patient groups has several implications. Individuals do not want to submit their personal data to many different registries; submitting data to multiple registries (national, regional, international) is also burdensome for treatment centres [5]. As a result, coverage may be inefficient. Collecting the same data for more than one registry wastes resources and may falsely inflate the number of patients affected. It may also be difficult to identify duplication when different data are collected, or collected in different ways, from individuals.

Data compatibility will be improved if core dataset elements can be agreed and harmonised [4,5,6]. At present, however, it is not clear how to persuade stakeholders to agree on a common protocol for data collection. Key players are likely to include information technology and technical partners who can find ways to help databases and registries 'talk' to one another, either through linkage or combining data. National health authorities, healthcare system funders and organisations that fund registries or pay to use them should be involved. The EHC is well placed to promote good practice at an international level.

Given the international scope and the variables inherent in resolving challenges around data harmonisation and access in European patient registries, a top-down strategy led by an external organising body may be the best approach to implementing potential solutions. Similarly, a step-by-step approach is recommended in order to avoid attempting too much too soon. The scope for passive data collection (i.e., collection of data without direct patient involvement) should also be explored.

2. DATA QUALITY

The challenge of data quality is inextricably linked with that of the multiplicity of registries and datasets described above.

The nature and quantity of data collected influences the accuracy with which data are recorded and the accessibility of information held by a registry. Similarly, mechanisms for collecting data will vary nationally and may even vary between treatment centres in a given country. Patients may be deterred by requests for a large amount of information [7], especially if they are involved in more than one registry [5], which poses a threat to the completeness of the dataset. Data managers should monitor data quality and have strategies in place to deal with missing or faulty data. Some personal data may raise particular privacy concerns, introducing a need for additional security requirements [8]. This has implications for registry owners and regulators, and related obligations on researchers who use the dataset. Organisations that fund registries must also consider

the costs associated with increasing the volume and sensitivity of data collected.

The purpose of a registry and its data requirements should be clearly defined, taking into consideration the many different needs of its stakeholders. For example, it is important to minimise the burden on patients who provide data for altruistic reasons when there are research demands for highly detailed information. Data managers are concerned with reconciling the needs of users (efficient access, data accuracy and consistency) with the requirements of regulators (data security and privacy) and may not be aware of the full range of issues associated with the disorder the registry is concerned with. This potentially indicates a need for focused professional development [5]. There is also a risk that the goals of different stakeholders may lead to a loss of focus in how the registry is managed, which again speaks to the importance of agreeing core datasets [4,5,6].

All end users should have a voice when striking a balance between data volume, quality and usability. Medical, scientific and patient communities are key actors in driving increased data quality through defining and developing which common data elements should be included in registries, to which specific information on specific questions can be added [5,9]. This in turn supports the interoperability of registries. Technical partners have a major role in developing easier ways to analyse data and support this crosstalk between registries. Regulators must be involved to mandate these changes, and it will be essential for national governments to be involved to ensure long-term funding.

Again, it is unlikely that effective change will be achieved quickly. Aiming for a basic level of data interoperability in the first instance is recommended. Lessons could be learned from how this has been approach in other disease areas, for example cystic fibrosis, where a European-level registry defines data variables [10].

3. DATA SHARING

The issue of who owns patient data in a registry is often omitted but is crucial. Patients may expect the right to access information about themselves or to receive information from a registry of which they are part. There are also questions that must be answered by organisations managing a registry. By which criteria do they permit researchers to access to the data? To what extent should organisations that fund a registry have control over the data? What is the role of national agencies in ensuring confidentiality while encouraging research that could potentially benefit the community?

If patients are to be encouraged to contribute to a registry, they must be able to trust that their data are managed properly with regard to security and privacy [4], and that access is granted when reasonably requested. The requirement for uniform good governance, with a suitable framework of laws and regulations governing registry activities, is therefore essential.

Patient organisations, registry holders, the medical community, national authorities and legal advisers should work together to find a common path forward and develop data transfer agreements that clearly set out what patients consent to when they provide information [9,11]. This will involve adaptation of established arrangements for some registries and the introduction of new standards for those currently without ownership rules or intellectual property agreements.

4. EXPANDING THE SCOPE OF REGISTRIES

This challenge also speaks to the need for interoperability between registries and datasets [12], and the associated need for effective governance to manage data sharing.

Identifying the questions that will be asked of a registry will vary depending on the stakeholder group involved, but it is important to understand what is expected. For example, will research questions be limited to data in the registry or is there a need for linkage with other datasets? How much data compatibility is required for the full potential of the dataset to be realised? In addition to ensuring effective linkage between registries to facilitate analysis, there is a need to consider data sources beyond that supplied by clinicians, including real-world and patient-reported data. However, the use of such data varies considerably between countries [13,14].

The challenge of registry scope impacts researchers, data managers, registry holders, regulators and funders because the scope of the registry will determine its costs, its value as a research tool, the investment required in terms of data input and compatibility, patient consent and the quality of data outputs. A clear understanding of the purpose and use of registries is required to ensure sustainable funding, continued motivation of the data providers and ongoing patient participation.

5. THE ROLE OF THE PATIENT IN REGISTRIES

As the individuals whose data is held in patient registries, patients are, of course, core to their purpose and function. Their role is multi-faceted and presents

a series of interlinked challenges. These include motivation to contribute to registries, the individual benefit of registry participation, and the need to add value to registries through inclusion of patient-reported outcomes (PROs).

Patients provide data to registries with little or no personal reward. To ensure their continued participation, it is vital that they see the relevance and value of continuing to contribute their data – without this, there is a risk that patients may become demotivated, with the loss of important insights. This is an issue that should be addressed jointly by patients, clinicians and data entry teams to define the outcomes of interest and scientific utility and ways in which patients can clearly understand and be incentivised to remain involved with registry participation. To that end, it is important to understand their motivations and what they value in contributing to a registry [15]. For example, do they see it as a way of being connected with their community, or as a source of information about their disorder?

Registry output is a two-way street: it is crucial to think beyond scientific endpoints of aggregated data and develop core outcome sets that make the registry relevant to the individual patient. As such, keeping patients up to date and ensuring that they are educated in respect of their condition is imperative. However, it is also important that, as key stakeholders, patients are part of any consortium that drives the next steps for registries. Despite PROs being of value to researchers, clinicians and patients, the lack of PRO data in registries is known to be a challenge [5]. Understanding patient motivations should be used to inform the development of PROs. This will help to ensure that patients remain involved in registry participation in the long term and will ultimately benefit patient care [16]. Technology companies can design solutions to make it easier for patients to track their data and can provide feedback. Registry holders should have oversight of this process to ensure regular review and to maintain impetus.

SUMMARY AND NEXT STEPS

Patient registries are an important tool for research and developing health care for people with rare disorders. The heterogeneity in the way that registries are designed, the type of data collected and the way data is collected are issues that must be addressed. Good, quality data is needed at all levels – regional, national and international – to ensure the provision and funding

THE EHC THINK TANK

The European Haemophilia Consortium (EHC) Think Tank was launched in June 2021. Building on existing advocacy activities, the initiative brings together a broad group of stakeholders who will engage with key thematic areas or workstreams identified as priority areas for "systems change" within European healthcare systems [17]. The EHC Think Tanks seeks to mobilise the agency and purpose of all stakeholders in the healthcare system to collectively design and champion potential solutions to existing problems.

The EHC steering committee was presented with more than 20 topic areas identified from patient, medical and scientific volunteers within the broad community. Following a prioritisation process in early 2021, three key topic areas were identified for Think Tank workstreams to tackle:

- Registries
- Hub-and-spoke treatment models
- Patient agency.

Workstream members are invited based on their expertise and potential for constructive engagement, including patient and industry perspectives alongside a balance of healthcare professional, academic, regulatory, governmental and geographical representation. All workstream activities are held under the Chatham House rule to enable inclusive and open discussion: participants are free to use the information received, but neither the identity nor the affiliation of the speakers, nor that of any other participant, may be revealed [18].

Each is project-managed from within its individual membership. Members will set their own agendas, timelines, and targeted outputs, with operational, logistical, methodological and facilitation support from EHC staff and Think Tank practitioners.

While concrete outcomes and results will vary across workstreams, they are likely to include (but not be limited to) manuscripts, consensus-based guidelines, monographs, white papers, and so on.

https://www.ehcthinktank.eu

of effective care, and data quality will increase overall if it is possible to merge data from different registries. The value of patient participation in registries must also be acknowledged and built on to ensure that patients remain motivated as active contributors.

The EHC Think Tank Workstream on Patient Registries has identified five key and interlinked challenges faced by providers, users and funders. The next step is to vet these challenges with a broader group of external stakeholders and bring their perspectives back into this workstream to expand understanding.

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