Five FAIR Neuromuscular Rare Disease Registries Now Provide Joint Answers to Questions from Researchers or Patients

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How many patients with rare neuromuscular disorders are there? How much time is there between the appearance of the first symptoms and the diagnosis of a rare disorder? These questions are highly relevant for patients but also difficult questions to answer. Most of the answers can be found in patient registries, but there are many different registries and, up to now, it was difficult to query these registries all at the same time. We now provide a proof-of-concept demonstrating how five different rare disease registries for neuromuscular disorders can now be jointly queried because they are interoperable, announced Peter-Bram 't Hoen, Professor of Bioinformatics at Radboud University Medical Center.

"We have made it easy for new FAIR registries to participate in joint analyses with other registries, answering questions around disease diagnosis, aetiology and progression. Patients can be assured that their data are being reused, in a secure manner, by scientists, clinicians, or other authenticated and authorised health professionals - which is their desire," *said Peter-Bram who is ERN EURO-NMD FAIRification and Interoperability Work Package Lead.*

This is the result of a close collaboration between different partners under an EU-grant proposal for ERN EURO-NMD, coordinated by a FAIRification team at Radboudumc. The registries that participated in this

proof-of-concept with mock data are: DDP (Duchenne Data Platform, patient-led registry for Duchenne and Becker Muscular Dystrophy, the Netherlands), CRAMP (Computer Registry of All Myopathies and Polyneuropathies, the Netherlands), DM-SCope (National registry for Myotonic Dystrophies, France), SMArtCARE (Clinical registry for Spinal Muscular Atrophy, Germany), and European Reference Network (EURO-NMD) registry.

Thanks to this important milestone, it is now possible to conduct the same queries related to neuromuscular diseases in multiple, independent registries simultaneously without exposing sensitive patient details. In order to support others in their FAIRification efforts, this demonstration prototype is publicly accessible in the Jupyter data analytics environment (https://github.com/markwilkinson/Duchenne-daru).

"One of the main ideas behind FAIR is for data to be both read, and 'understood', by machines. Achieving this has significant benefits for highly sensitive data, since it allows us to send machines into private data spaces to do the exploration and analysis for us, without needing to expose that data to a person. This is what we demonstrated in this proof-of-concept: machines could execute complex analyses entirely on their own, over multiple patient registries, while keeping the sensitive data completely protected at all times." *- Mark D Wilkinson, co-Founder of FAIR Data Systems and lead-author of the original paper describing the FAIR Data Principles.*

FAIR stands for Findable, Accessible, Interoperable, and Reusable. It is the acronym used to describe a global initiative to make data more valuable by increasing the ability of computers to find, interpret, integrate, and analyse those data autonomously. In this prototype, the computer calls a special Web address where specified and pre-approved queries (e.g. patient-count or phenotypic observations) are executed inside the FAIR registry's secure space, and anonymized data are given back to the computer as output (see Figure below). The prototype depends on a publicly available database of queries that were manually curated and filtered by experts in FAIR and neuromuscular diseases. FAIR makes it possible for the same query to be executed over independent resources, and thus sharing those queries leads to convergence between registries.

The next steps are to increase the number and sophistication of the publicly available queries - all reviewed for security by both technical and rare disease experts - in the demonstration prototype.

More specifically, patients and families living with Duchenne or Becker Muscular Dystrophy will be able to ask questions that matter to them such as 'How many people have the same symptoms as me?'. The proof-of-concept will make it possible to send this question or 'query' across other FAIR registries within the ERN EURO-NMD registry Hub, with a reach of an estimated 100,000 patients with neuromuscular diseases. Up-to-date and instant results will be received automatically which saves time and valuable resources. This ultimately, helps progress towards earlier diagnosis and innovative treatments.

"The quote by Nelson Mandela, 'It always seems impossible until it's done' couldn't be more appropriate in achieving this milestone. Managing five different teams and the FAIR experts required focus, resilience, flexibility, and an incredible determination by everyone involved. Prototypes work wonders in 'showing' various stakeholders how we're creating impact with FAIR data. Today, we're being assisted by machines to access high volume data, stored in different locations and get answers to specific validated predefined questions, all automatically within seconds," *explained Nawel Lalout, FAIR project manager at the World Duchenne Organization who coordinated these efforts to completion.*

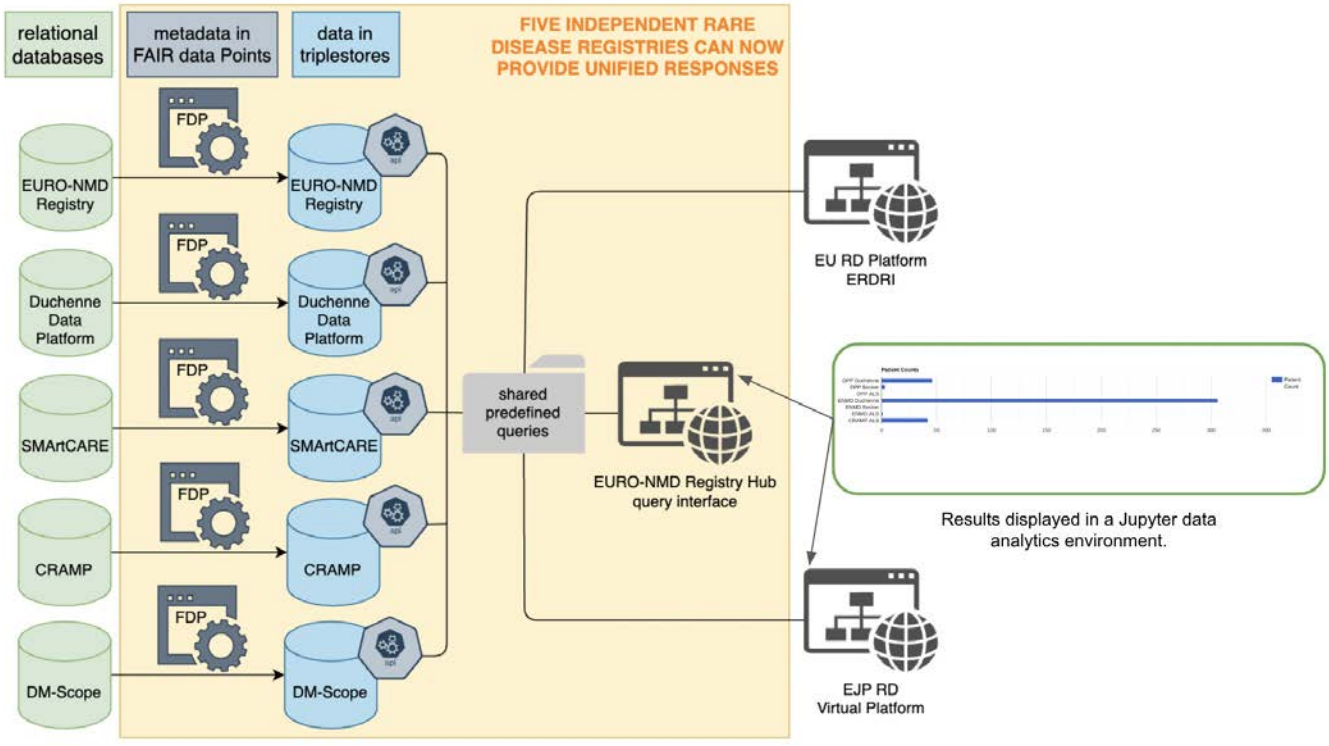

Figure. Schematic representation of the privacy-preserving federation over multiple, independent registries. *Queries are executed, on demand, over FAIR datasets through a query interface. All of this is protected by a "proxy", which further insulates the other components, and ensures only encrypted communication over the Web. Accessing the proxy retrieves, for example, only a count of patients with a given rare disease that can be aggregated in a graphical analytics environment. [Abbreviations: API, Application Programming Interface; FDP, FAIR data point; EJPRD, European Joint Program on Rare Diseases]*

For any additional information, please reach out to Nawel Lalout, FAIR Project Manager, World Duchenne Organization at nawel.lalout@worldduchenne.org.

About Duchenne Parent Project (DPP)

The Duchenne Parent Project, a patient advocacy group in The Netherlands, was founded in 1994. It strives to raise awareness, accelerate research to find a cure, improve treatments, and optimize access to care for everyone with Duchenne and Becker Muscular Dystrophy. Their commitment to implementing the FAIR Guiding Principles for Scientific Data Management and Stewardship started in 2019 soon after the World Duchenne Organization published the Duchenne FAIR Data Declaration. Their journey with FAIR continued under their patient-led registry the Duchenne Data Platform achieved a FAIR status within one year; followed by demonstrating interoperability with ERN EURO-NMD six months later and now with this proof-of-concept, they aim to encourage more Duchenne patient organizations to join their FAIR efforts so that together that can optimise the (re)use of all Duchenne and Becker data collected and stored in different data sources.
For more information, visit https://duchenne.nl.

About ERN EURO-NMD

EURO-NMD is a European Reference Network (ERN) that aims to harmonise and implement best practices for clinical and diagnostic procedures for rare neuromuscular diseases across all European Union member states. EURO-NMD, the ERN for Rare Neuromuscular Diseases, spans 24 European countries and includes 85 reference centres. EURO-NMD oversees more than 100,000 patients with rare neuromuscular conditions. The Network members are committed to collaborating closely to improve the health outcomes of their paediatric and adult patients with rare neuromuscular disorders. Core objectives of the collaboration are the implementation of clinical practice guidelines and the definition and prospective monitoring of core indicators of guideline conforming management, treatment quality and patient health outcomes.
For more information visit https://ern-euro-nmd.eu.

About FAIR Data Systems

FAIR Data Systems S.L., Madrid, (FDS) is a leading consultancy company in planning, building, and providing training in FAIR-compliant data systems. In this initiative, FDS engaged with the DPP FAIR Data Stewards to rapidly deploy a FAIR solution for the Duchenne Data Platform, which was then provided as an open source solution to the European Joint Programme on Rare Disease, where it was further refined and made more robust. FDS designed and established the shared-query concept, and its governance - referred-to as “data visiting”. This approach leverages the power of FAIR data to enable queries to be automatically executed inside the registry’s protected space without any need for human involvement, thus minimizing the time and expertise required by the data host. FDS also has ISO-certified and GDPR-

compliant servers for hosting sensitive medical data for clients who are unable to host FAIR databases, or FAIR data transformation software, on their own.
For more information visit https://fairdata.systems/home/.

About Radboud University Medical Center (Radboudumc)

It was founded in 1956, is the teaching hospital affiliated with the Radboud University Nijmegen, in the city of Nijmegen in the eastern-central part of the Netherlands. It is one of the largest and leading hospitals of The Netherlands with about 1,000 beds. The medical center's infrastructure consists of several technology centers and three research institutes: Radboud Institute for Molecular Life Sciences, Radboud Institute for Health Sciences and the Donders Center for Medical Neuroscience within the Donders Center for Brain, Cognition and Behaviour and several technology centers. The scientists perform cross-disciplinary research regarding 18 clinically relevant research themes. They have created successful innovations in the fields of prevention, diagnostics and treatment based on years of scientific research. They have extensive resources and expertise to facilitate the interoperability of the registries and therefore are involved in the EURO-NMD Work Package for FAIRification and Interoperability under the leadership of Peter-Bram ‘t Hoen, Professor of Bioinformatics at Radboud University Medical Center.

Acknowledgements

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