WEBINAR REPORT

Improving Rare Disease Real-World Data Quality and Availability for HTA/Payers

Wednesday, 8 April 2026, 15:00-16:30 CEST

Keynote speaker

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Coordinator, European Reference Network for Rare Hereditary Metabolic Diseases (MetabERN)

Speakers

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Executive Director, Canadian Neuromuscular Disease Registry)

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EXECUTIVE SUMMARY

On 8 April 2026, the RWE4Decisions webinar on **"Improving Rare Disease Real-World Data Availability and Quality for HTA/Payers"** brought together perspectives from clinical networks, industry, patient organisations, and HTA bodies to explore how real-world data (RWD) and registries can better support decision-making for rare diseases.

Rare diseases present persistent challenges for evidence generation due to small patient populations, limited clinical data, and uncertainty around meaningful outcomes. While innovative therapies are increasingly available, the supporting evidence base for HTA and payer decisions often remains limited. Across the discussion, speakers agreed that the priority is to ensure that data is **reliable, interoperable, decision-relevant, and governed in ways that support multiple uses** across research, regulation, HTA, reimbursement, and patient care. Registries were highlighted as a critical part of this infrastructure, but also as systems that must evolve through strengthening **governance, incentives, collaboration, sustainability, and trust**. The discussion pointed to a unique policy moment in Europe, where the development of the European Reference Networks (ERNs), the European Health Data Space (EHDS), and the proposed Biotech Act create a major opportunity to strengthen rare disease data ecosystems and improve access to therapies.

SETTING THE SCENE: WHY RWD MATTERS FOR RARE DISEASES

Victoria Hodgkinson (Executive Director, Canadian Neuromuscular Disease Registry), co-moderator, set the scene for the discussions by framing **rare diseases as one of the most profound challenges in modern healthcare**. Although 300 million people around the world are living with a rare disease, fewer than 5% of the approximately 7000 rare conditions have an approved treatment. Even when therapies are available, the evidence base is often limited by small trial populations, short follow-up periods, or endpoints that may not fully capture what matters most to patients and their families.

The challenge is not simply collecting data, but ensuring that the data collected are **the right data, structured in the right way, and capable of informing the decisions that matter**. Broader international registry collaboration has shown both the potential of registries to generate long-term evidence and the difficulty of adapting existing systems to new requirements for interoperability, data quality, and HTA.

A key challenge **is the gap between the registries and data systems that exist today and the evidence that HTA bodies and Payers need to make confident, timely coverage decisions**. Retro-fitting long-standing registries, or differing registries from a wide range of countries, to serve data-sharing, interoperability, and decision-making purposes is a slow and demanding process, but one that is essential for rare disease data to support decisions.

This set the scene for a discussion focused not only on what is possible, but on what needs to change.

KEYNOTE: INNOVATING DATA COLLECTION ACROSS STAKEHOLDERS TO DELIVER VALUE IN RARE DISEASES

"It is a golden moment for rare diseases, after how much we've done in understanding what rare disease is and how to develop therapies and improve diagnosis", said **Prof. Maurizio Scarpa** (Coordinator, European Reference Network for Hereditary Metabolic Disorders (MetabERN)). However, he noted that major challenges remain: rare diseases are geographically dispersed, and data collection and registries remain fragmented and insufficiently interoperable.

Europe already has a large number of rare disease registries, yet they often operate in isolation and cannot easily be combined for research or decision-making. Europe now has both the experience and the political opportunity to transform existing infrastructures so that health data can be used more effectively to improve outcomes and quality of life.

A major foundation for this work is the **European Reference Networks (ERNs),** created in 2017 to support cross-border collaboration and bring expertise closer to patients. The 24 ERNs now connect more than 1,600 specialised units and nearly 400 hospitals, and each ERN is associated with a registry infrastructure, including disease-specific and broader rare disease data systems. Prof. Scarpa highlighted MetabERN's Unified Registry for Inherited Metabolic Disorders as an example of a pan-European registry that is designed not just as an administrative database, but as a living scientific tool capable of supporting multiple stakeholders, including regulators, HTA bodies, Payers, clinicians, and patients.

ERN registries are aligned around **common data elements** and the **FAIR principles** (findable, accessible, interoperable, and reusable). This enables longitudinal natural history studies, virtual consultations, and cross-border case comparisons, which in turn feed into regulatory and HTA submissions, post-authorisation studies, and managed entry agreements. However, challenges include high data-entry burden on clinicians, insufficient support and funding for registry work, limited feedback to data contributors, heterogeneity in standards across national and disease-specific registries, and unresolved governance questions around access, control, and reuse. Efforts are currently ongoing to address these barriers through the creation of consortia of national institutes of health, to encourage wider use of registries and better data management among researchers, clinicians, and patient advocacy groups.

Prof. Scarpa then focused on the changing European policy context. He explained that the **EU HTA Regulation** can create a formal demand for RWE from ERN registries, especially in JCAs and reimbursement settings. At the same time, the **European Health Data Space (EHDS)** provides a legal framework for secondary use of health data, including cross-border access, data linkage, and common interoperability standards for Health Data Access Bodies, creating the possibility of moving rare disease RWD from aspiration to a practical reality.

Prof. Scarpa also highlighted the recent **Health Leadership Mission for Rare Diseases**, which brought together all 24 ERNs with policymakers, patient organisations, industry, HTA bodies, and Payers. This initiative identified eight key strategic priorities, which are now being developed. One

such strategic priority is the creation of a **comprehensive rare disease infrastructure cluster**, which can be summarized into six points:

1) Sustainable ERN funding
2) Integrated data ecosystems connected between national registries, ERN registries, and EHDS, and adopting the FAIR principles
3) Accelerated diagnostics and reusage of data for AI use in a cross-border way
4) Equitable access to therapies
5) Patient-centred research, embedding patient-reported outcomes and patient co-design
6) Alignment with the forthcoming **Biotech Act**

Regarding the synergies between the EU **Biotech Act** for rare diseases, Prof. Scarpa highlighted its ambition to streamline clinical trial authorisation across Member States. A more harmonised European framework could reduce delays, support a unified platform for trials, and improve Europe's capacity to study rare disease treatments. When combined with RWE from registries, this could support both regulatory and HTA decision-making. Taken together, Prof. Scarpa argued that the ERNs, EHDS, and Biotech Act could create a transformative ecosystem for rare diseases: ERNs provide the clinical and registry infrastructure, the EHDS provides the legal and interoperability framework, and the Biotech Act could enable practical implementation at scale.

He concluded that realising this vision will require **strong multi-stakeholder collaboration**, and ended with a series of questions that should guide the further actions of each stakeholder group:

- **HTA/Payers:** How can we formally embed the registry data requirements into HTA process for rare diseases? What governance structures will ensure data quality and independence?
- **Patient organisations:** How do patients move from data contributors to data co-owners? What is the mechanism ensuring that patient groups receive meaningful feedback on the data they provide?
- **Industry:** When no robust RWD system exists, what is the industry's responsibility to build one? How can pre-competitive collaboration be structured under the EHDS and the Biotech Act?
- **ERN clinicians:** How can we design the next generation of registries to serve HTA/Payer needs without compromising clinical utility? What resources and recognition are needed to sustain physician engagement?

His final message was that the rare disease community is in a uniquely strong position to act. The challenge is not primarily technical: it is a matter of governance, incentives, and collaboration. With the right policy support, RWD can become a practical tool to improve diagnosis, evidence generation, access to therapies, and ultimately quality of life for people living with rare diseases.

MULTI-STAKEHOLDER PANEL DISCUSSION

The keynote presentation was followed by a series of introductory remarks from HTA bodies, patient, and industry representatives. This section sets out to gather a multistakeholder perspective on how rare disease RWD availability and quality can be improved to support HTA/Payer decisions.

The use of RWD for developing rare disease medicines

Alessio Amadasi (Chiesi Group) began by offering the industry's perspective of how RWD can be used throughout the lifecycle of development for rare disease medicines.

Before clinical development, RWD can be used to **characterise the natural history of the disease, identify unmet needs, and support the design of clinical studies**, particularly the selection of study endpoints that matter to patients and caregivers. Of particular relevance for rare and ultra-rare diseases, registries can help identify *where* patients are being followed and managed, what is the population size, and which clinical sites may be involved in development.

During clinical development, RWD and RWE can provide **information to supplement randomised controlled trials** (RCTs). In situations where these are difficult due to low patient numbers, high-quality RWD and registry data may enable the use of external comparator arms, providing a control to what is observed in patients undergoing therapy in interventional, single-arm control studies. Mr. Amadasi illustrated this with an example of treatment for Leber's Hereditary Optic Neuropathy, where natural history data was used to provide confirmatory efficacy evidence generation for an interventional study.

In post-approval settings, RWD enables the **collection of long-term efficacy and safety information**. For example, patients previously enrolled in clinical trials can be followed without the need for open-label extension interventional studies, reducing the burden on patients, clinicians, and the developer, and allowing the collection of long-term data in registries. These are increasingly used to fulfil post-approval commitments, and they can also capture outcomes not easily measured in trials, such as patient and caregiver perspectives, including impact of therapy on patients' self-care and mental health.

In closing, Mr Amadasi's key message was that **RWD represents a good opportunity for industry to generate more evidence to complement clinical trials**. However, **the value of the data depends on proper methodological approaches and understanding the perspectives of different stakeholders to ensure that the evidence is fit for purpose.**

Patient involvement in RWD collection for rare diseases

Regarding patient involvement in RWD collection, **François Houÿez** (EURORDIS) argued that they should be involved not only in collecting evidence, but also in **shaping what the registries collect, how they are governed, and which guidelines apply.** Based on experience from clinical trials and registries, patients can help identify which treatments are most appropriate for specific populations, lines of therapy, and subgroups. This knowledge strengthens their contributions to HTA, including by shaping research questions, defining PICOs, and informing the design of clinical

trials and JCAs. However, this level of engagement depends on the **availability of high-quality, standardised data**. Currently, significant variability exists across registries and centres of expertise, making it difficult for regulators and HTA bodies to interpret and use the data efficiently. Patient organisations can play an important role in **identifying these inconsistencies and advocating for greater standardisation across registries**.

A further priority he indicated is **stronger patient involvement in registries' governance.** An analysis of the EMA catalogue of RWD sources uncovered that only a minority of them involve patients in their governance. For ERNs, 66% do, but many consent processes are still developed without patient input, which may contribute to high non-participation or dropout rates. Mr Houÿez pointed out that in some ERN registries, up to 40% of patients decline for their data to be included, potentially reflecting poorly designed consent mechanisms.

Mr. Houÿez also emphasised that health data should be considered a public good, and that the priority should therefore be to involve patients in governance structures that determine **who can access data, for what purposes, and under what conditions.** In this model, patients act as partners in decision-making rather than passive contributors.

Finally, he stressed the importance of **closing the feedback loop**. Patients who contribute data should **receive clear, accessible information on how it is used and what insights are generated**. Strengthening these feedback mechanisms is essential to build trust, improve participation, and maximize the value of RWD.

Where and how can RWD be used In HTA?

Prof. Wim Goettsch (ZIN) confirmed that RWD is used in HTA, but emphasised that the key question is **where and how** it can be used across the medicine lifecycle.

In the Netherlands, disease registries are an important source of evidence for **horizon scanning**. They help identify emerging treatments, estimate prevalence and incidence, and understand current treatment patterns. This information supports early multistakeholder discussions to assess what evidence will be needed to prepare for future decisions. Registry data can also inform the design of clinical trials and JCAs, for example by identifying relevant comparators and outcomes from an HTA perspective.

Once treatments are in routine use, registries become valuable for monitoring **appropriate use**: who is being treated, whether outcomes align with expectations from clinical trials, and what the overall effectiveness is. For example, in the Netherlands, the patient-led cystic fibrosis registry and the HemoNED haemophilia registry have been used to understand treatment effectiveness, long-term outcomes, and how new medicines are replacing existing treatments. However, he noted that it remains difficult to measure the direct impact of registry evidence on reimbursement decisions and prescribing behaviour in clinical practice.

Registries also have an important role to play in **conditional reimbursement**, particularly for very rare diseases. In these cases, a treatment may be reimbursed while additional evidence is collected. For example, in metachromatic leukodystrophy, the conditional reimbursement for

juvenile early symptomatic patients is based on an international registry, as patient numbers are too small for clinical trials or a national registry alone to generate sufficient evidence.

Finally, Prof. Goettsch discussed the use of registries in initial HTA assessments. While HTA bodies generally prefer RCTs, this may not always be feasible for rare diseases. In such cases, single arm trials may be used, matched to external control arms based on registry data. However, this must be planned carefully: registries should not be an afterthought, but designed and used in ways that ensure comparability, matching, and data quality for decision-making.

Canada's efforts to strengthen the role of registries in decision-making

Dr Nicole Mittmann (CDA-AMC) described recent efforts in Canada to strengthen the role of registries in decision-making. These include a **funding stream under the national rare disease strategy**, an initiative which aims to improve the **quality, governance, and usability of rare disease registries**, enabling them to better inform HTA and policy decisions.

She noted that registries are an important tool to connect small or underserved patient communities. However, using registries to inform HTA requires additional steps: this includes **strengthening governance structures, improving consent processes,** and **ensuring collection of consistent, decision-ready data**. Consideration must also be given to **increasing enrollment in registries,** capturing **sub-populations that are underrepresented in RCTs**, and collecting a broad range of **decision-relevant outcomes** (e.g. clinical outcomes, resource outcomes, patient-reported outcomes).

Dr Mittmann also highlighted the importance of foundational work to support the use of registry data, including developing **roadmaps for linkage and access**, improving interoperability, and ensuring effective integration into decision-making processes. She pointed to Canada's **assessment criteria for RWE**, which recognise that HTA relies on comparative analysis and that appropriate methodologies and outcomes must be defined to support this. Another key theme was the importance of **multi-stakeholder collaboration**, bringing together patient groups, caregivers, industry, and data holders to ensure that the right data are collected and that outcomes reflect what is meaningful to patients and health systems.

To illustrate the above, she pointed to two of CDA-AMC's initiatives: firstly, a value framework for deliberation that incorporates clinical, unmet need, economic, societal and ethical, and system-level considerations, where registry data and RWD can provide important contextual evidence. Secondly, a **lifecycle (sandbox) programme**, which allows the assessment of technologies that are already in use, but which have not undergone a formal HTA due to limited data, and which would benefit from using RWE from sources such as registries and databases.

In closing, she clarified that RWE is currently used primarily to **support and inform decision-making.** However, its role is growing, particularly in providing context and complementing other forms of evidence.

MODERATED Q&A DISCUSSION

Building onto the introductory remarks, a moderated Q&A session followed, where the speakers responded to the following questions from the audience and the co-moderators:

- How do we ensure the collection of sufficient data to be able to inform decision-makers without making it overburdensome on clinicians or patients, taking into account the heterogeneity of rare diseases and of the decision-makers' needs?
- Which communities should have access to registries, and how should this work in practice?
- How can we incorporate patient-reported outcomes and quality of life metrics into registers, and what is the value of that in decision-making?
- Are there new digital technologies that would assist our data collection, governance, and use?

Several important takeaways emerged from the discussion. Firstly, regarding the **balance between data completeness and feasibility**, a common recommendation was to define a **minimum core dataset or core outcome set**, developed collaboratively across stakeholders, and to allow registries to evolve over time through modular additions (e.g. treatment-specific modules). This approach enables registries to remain relevant while avoiding excessive burden.

Secondly, the importance of **interoperability and standardisation** was strongly highlighted. To combat the different definitions and data collection practices across registries and countries, panellists stressed the need for alignment on common standards and the use of existing data sources to minimise duplication and reduce workload.

Thirdly, registries were recognised as critical tools for understanding **real-world effectiveness, patient heterogeneity, and treatment pathways**. Registries can complement clinical trials with additional long-term outcomes and variation in patient responses, supporting more informed decision-making. However, speakers noted that the impact of registry data on clinical practice and reimbursement decisions requires further evaluation.

The panelists also agreed that **clearer and more transparent mechanisms for accessing registry data** are needed. The health data access bodies emerging under the EHDS are expected to play a role in enabling structured and equitable access for stakeholders, including patient organisations and HTA bodies, while safeguarding the public interest.

Patient-reported outcomes and quality of life data are important for capturing aspects of disease burden that are not reflected in clinical trial endpoints. These data are particularly valuable for informing HTA deliberations on unmet need, equity, and patient impact. However, challenges remain in selecting appropriate measurement tools, ensuring consistency across registries, and integrating these data into decision-making frameworks.

Looking to the future, speakers highlighted the potential of **digital technologies and data integration**, including structured electronic health records, standardised coding systems, and artificial intelligence. These tools could improve data quality, reduce manual data entry, and enable earlier diagnosis through advanced analytics. However, their implementation will require investment, training, and greater awareness among clinicians.

Finally, the discussion underscored the importance of **education and capacity-building**, particularly for clinicians and patient representatives, to ensure that data are collected, interpreted, and used effectively.

In closing, the panellists reflected on how their stakeholder group can better support the use of RWD in decision-making. Across the stakeholder groups, the importance of **multistakeholder collaboration** and **improving the accessibility, quality and interoperability of patient registry data** emerged as central themes. In terms of targeted actions, the panellists called for:

- Early and continuous collaboration between stakeholders to define evidence needs and align on data collection from the outset
- Development and adoption of **core datasets and standardised methodologies** to improve comparability and usability of registry data;
- Greater investment in registry infrastructure and sustainability, recognising registries as critical scientific assets;
- Strengthening **patient involvement in governance** and improving feedback loops to maintain engagement and trust;
- Enhanced **training and capacity-building** for clinicians, patient advocates, and decision-makers on the use of RWD;
- Improved methodological approaches for using registry data in HTA, including for comparative analyses and effectiveness studies;
- Leveraging existing European initiatives and policy frameworks to accelerate progress and ensure coordinated action.

RWE4Decisions REAL WORLD EVIDENCE

RWE4Decisions is a payer-led multi-stakeholder learning network, which has developed **stakeholder actions** that will better enable the use of real-world evidence in HTA/payer decisions about highly innovative technologies.

RWE4Decisions brings together experts from all stakeholder groups to engage in dialogues that consider how fit-for-purpose RWE can be generated over the life cycle of **highly innovative medicines** through:

- horizon scanning systems that identify medicines which are most likely to need RWE
- identifying what RWE is needed to inform HTA/Payer decisions
- clarifying how RWE should be generated by stakeholders and evaluated by HTA/Payers
- aligning planning and execution of effective Post Launch Evidence Generation (PLEG) studies.

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For further information and to watch the recording of the webinar, visit our **website**.

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