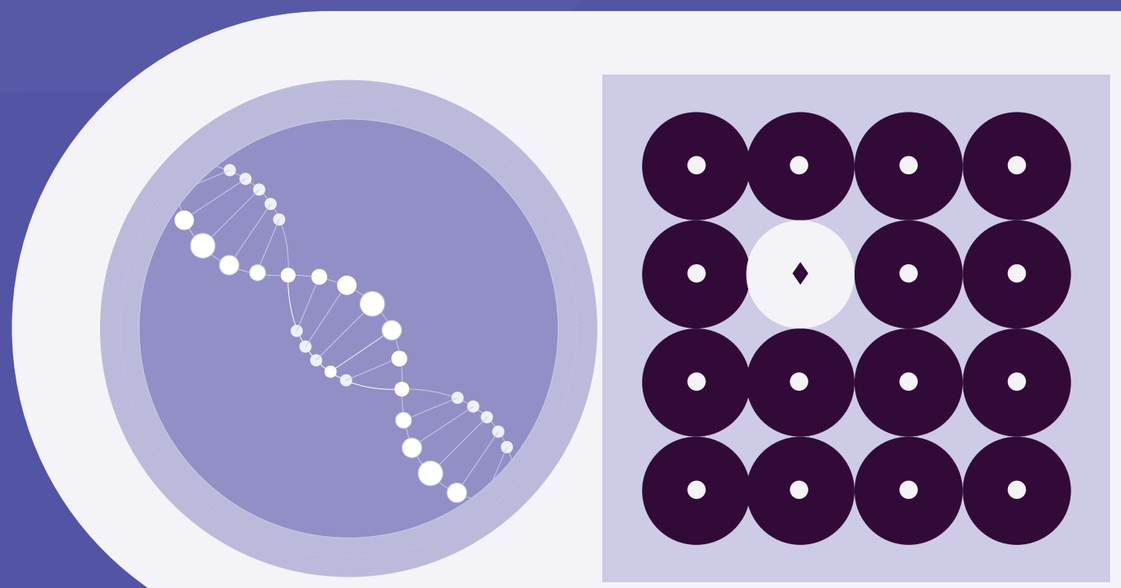
Harnessing
Real-World Evidence:

2025
Report

Empowering the Rare Disease Community



Insights From a Roundtable Discussion

Contents

Understanding Real-World Data and Real-World Evidence

What are RWD and RWE?

Real-world data (RWD) includes any health-related information collected outside of controlled clinical trials. For example, RWD can be collected from electronic health records, insurance claims and patient registries.

Real-world evidence (RWE) in healthcare refers to the insights derived from analysing RWD to understand how treatments work in real-world settings, supporting improved patient care and informed treatment decisions.

How Can You Generate or Access RWD?

The rare disease community are a key part of generating RWD; the perspectives of patients and caregivers, including their experiences, preferences, and support needs, are vital for ensuring that RWD provides a true and complete picture of the rare disease landscape.

Generate

- Establish patient registries
- Organise patient surveys and collect community feedback
- Participate in studies and patient focus groups

RWD

Access

- Collaborate with researchers
- Liaise with healthcare providers to utilise electronic health records
- Access publicly available databases

Key Concept

Patient Registry

A patient registry is a database that collects and stores information about individuals with a specific condition or disease. It helps track how the disease affects them over time by collecting information on patients' symptoms, treatment experiences and outcomes.

Why Are RWD and RWE Important?

Analysing RWD can provide important evidence for progressing improvements in patient care, for example, through informing changes to prescribing, funding, policy and patient support. Crucially, it reflects patients' experiences in the real world and therefore provides information across a greater range of people and situations, beyond what could be included in controlled research studies.[1, 2]

Whilst this is not an exhaustive list, some examples of the benefits of analysing RWD include:

Insights

RWD provides information on disease progression and patient characteristics, which can contribute to enhanced understanding of the disease and inform future research priorities

Support

RWD helps identify patient groups and enhances community networks, fostering collaboration and resource sharing among stakeholders

Regulatory and Policy

RWD supports regulatory and policy decisions by providing evidence on treatments or management approaches in real-world settings, leading to improved and more patient-centred care

Case Study

The Chronic Granulomatous Disorder (CGD) Society

The Chronic Granulomatous Disorder (CGD) Society provides support to individuals and families affected by CGD, and the professionals who support them. CGD is a rare, life-threatening and life-limiting genetic condition, usually diagnosed in childhood, that has severe consequences for those affected.

Key RWE Objective:

To use population health data to develop target-based strategies and advocate for improved access to healthcare and treatments for people with the disease.

Challenges

1. No registry or geographical map of people with CGD
2. Limited information available about the patient pathway
3. Lack of disease awareness in community healthcare

Key Concept

Patient Pathway

A patient pathway describes a person's journey through the healthcare system for managing a specific health condition. It typically includes diagnosis, treatment and follow-up.

Key Discussions and Recommendations

1. Map rare disease centres, establish a membership database and leverage existing resources/models to guide future activities

2. Map the patient pathway

- Conduct a medical chart review
- Refer to the society membership database
- Consult a nurse with CGD experience
- Establish a working group to explore the CGD pathway
- Develop a registry to document the experiences of people with CGD and clinicians

3. Influence primary care and educate about CGD

- Develop a library of direct-to patient information to support treatment in the community
- Employ nurses to educate their peers and empower patients to advocate for their community
- Connect with other charities; share experiences, contacts and influence

Plans and Progress

- We initiated the development of a comprehensive three-year strategy, incorporating key learnings, identifying new opportunities, and addressing potential challenges
- We started a thorough assessment of our nursing services, exploring opportunities for sharing best practices and enhancing knowledge around CGD
- We are utilising more extensive data sources to deepen our understanding of the population health implications of CGD, and to identify areas where we can provide additional support
- We are reviewing our partnerships and exploring ways to strengthen collaborations across the rare disease community
- We are enhancing our community engagement strategies to ensure our initiatives align with the needs of those affected by CGD, while advancing our mission and objectives

Wayne Kitchener
Chair of Trustees,
CGD Society

Case Study

SLC6A1 Connect UK-AQ

SLC6A1 Connect UK-AQ supports research and development, funding and networking, and helps translate science for people with *SLC6A1*-related disorders. Mutations in this gene can cause a spectrum of neurodevelopmental conditions, manifesting as ranging severities of developmental delay and cognitive impairment, refractory epilepsy, motor disorder, and speech and language delay or absence.

Key RWE Objective:

To generate publishable real-world data to encourage medicine regulators to support off-label use of a repurposed drug (glycerol phenylbutyrate) for *SLC6A1*-related disorders.

Challenges

1. Understanding the regulatory pathway and role of RWE within this
2. Identifying people with *SLC6A1*-related disorders
3. Collecting high-quality data from individuals using drugs off-label for *SLC6A1*-related disorders, ensuring it meets regulatory and publication standards

Key Concept

Drug Repurposing

Drug repurposing is the process of finding new uses for existing drugs. It involves researching drugs approved for one condition (on-label use) and testing their effectiveness for others. A drug that is used to treat a condition that it does not have approval for is known as off-label use.

Key Discussions and Recommendations

1. Identify new paths to rare disease treatments

- Liaise with regulatory and industry experts to understand the pathways for repurposing drugs, and identify ways that RWE can support the process
- Connect with stakeholders to explore investment opportunities with interested parties
- Explore the advantages and disadvantages of different routes to market. For example, off-label prescribing versus on-label routes such as the ‘Early Access to Medicines Scheme’ in England

2. Expand your network and use patient registries

- Map stakeholders to identify clinician and patient networks, reaching beyond immediate contacts to broaden reach and engagement
- Establish a central registry for data collection and collaborate with other organisations to link registries, pool data and combine resources

3. Conduct a RWE study

- Obtain informed consent from participants and ensure the study is approved by relevant ethics committees
- When designing the study, use relevant randomised controlled trials (RCTs) to define methods and key endpoints
- Select a study design that ensures high data quality. For example, include a control arm with participants matched by age and sex
- Maintain clear documentation of data collection and processing methods, to ensure data transparency

Plans and Progress

- We submitted an application to repurpose glycerol phenylbutyrate for people with *SLC6A1*-related disorders in the UK
- REMEDi4ALL are conducting their own investigations and communications to find innovative ways to obtain equitable and reimbursed access across Europe
- We begun work on a RWE study, creating a patient survey, and recruiting prescribing doctors. We aim to collect data from the largest published patient cohort to build a robust dataset for providing evidence of efficacy and safety
- We liaised with the British Paediatric Neurology Association (BPNA) to discuss how they could assist us in finding more people with *SLC6A1*-related disorders in the UK

Lindsay Randall
Founder and CEO,
SLC6A1 Connect UK-AQ

Case Study

Timothy Syndrome Alliance (TSA)

Timothy Syndrome Alliance (TSA) focuses on improving diagnosis rates, treatment, and support worldwide for individuals with *CACNA1C*-related disorders including Timothy Syndrome and LongQT8, while also aiding their families and caregivers. These disorders present with a spectrum of cardiovascular, endocrine and neurological/neurodevelopmental symptoms.

Key RWE Objective:

To understand if barriers to reporting are masking cases of rare diseases, specifically *CACNA1C*-related disorders, in the UK.

Challenges

1. Lack of communication and coordination amongst stakeholders
2. Establishing partnerships with influential organisations and collaborating towards joint success
3. Lack of a standardised recontact policy regarding genetic variants of unknown significance (VUS),[3] which leaves some patients unaware of the potential health implications of their genetic screening results
4. Raising awareness of VUS and using RWE to gain interest and advocacy
5. Presenting RWE in an impactful way to engage policymakers and stakeholders

Key Concept

Variants of Unknown Significance (VUS)

Variants of Unknown Significance (VUS) are genetic changes with unclear health impacts, meaning it is uncertain whether they contribute to disease or are harmless variations. They are identified through genetic testing.

Key Discussions and Recommendations

1. **Organise an advisory board** with clinicians from various regions to discuss best practices on reporting VUS and gather consensus
2. **Partner with organisations** to pool resources for larger, impactful initiatives. For example, collaborate with the cardiac community when genes associated with cardiovascular risks are a concern, to enhance awareness and understanding of VUS
3. **Develop resources** to raise awareness about reporting VUS among patients, healthcare providers, and key stakeholders for genes where screening could impact patient outcomes
4. **Engage a champion**, such as a political advocate, to elevate the profile of issues related to the lack of a standardised recontact policy for VUS. For example, by addressing them in parliament and challenging current practice
5. **Use qualitative and quantitative data to craft compelling narratives** for communication with external stakeholders, and create visually impactful resources that clearly define the issue and key takeaways for the audience

Plans and Progress

- We are drafting a language consensus manuscript to clarify the language relating to *CACNA1C* and the need for multisystem screening
- Our *CACNA1C* portal is being developed to serve as a comprehensive resource for all known data related to *CACNA1C* disorders. The portal will integrate data from clinical studies, research publications, and our *CACNA1C* patient registry
- We are finalising work on a project with Illumina, exploring the paths families take to obtain a diagnosis. We intend to share the recommendations from this research in a slide deck
- Our collaboration with gene groups and researchers via The Voltage Gated Calcium Channel Collective (VGCCC) continues, with the aim of raising awareness and advancing understanding of calcium gene changes and their associated pathogenicity

Sophie Muir
Founder and Chair, Timothy Syndrome Allliance (TSA)

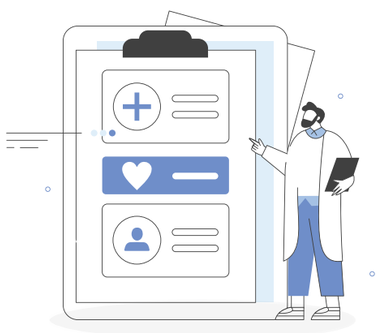
Maximising the Impact of RWE in Rare Diseases

Patient Registries

Patient registries serve as central databases that collect and store data from the patient community. By gathering comprehensive data on patient symptoms, treatment experiences and outcomes, registries provide valuable insights into disease course and inform research, ultimately enhancing treatment and care.

What can we do to maximise the impact of patient registries?

- Encourage related organisations, including healthcare providers, to signpost people diagnosed with a rare disease to the registry to extend the coverage and relevance of data across the rare disease population
- Ensure data collected via the registry aligns with your research objectives and uses validated scoring methods for assessing patient-reported health outcomes, such as the EQ-5D, that meet the requirements for publication or use in regulatory activities
- When establishing registries, add an option for participants to consent to be recontacted, providing the opportunity for involvement in future research
- Partner with researchers to share insights from the registry, ensuring continuous collaboration and maintaining community involvement in ongoing research efforts

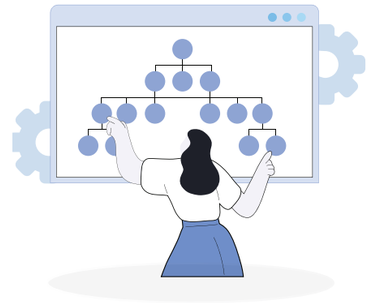


Stakeholder Mapping and Partnerships

Identifying and mapping stakeholders is crucial for establishing effective partnerships. By understanding the roles and interests across stakeholders, organisations can collaborate efficiently, align goals, and leverage resources to drive research and support efforts forward.

How can we engage stakeholders strategically to build partnerships and enhance research?

- Map stakeholders and understand their key goals and objectives to identify potential opportunities for collaboration
- Organise networking events to improve understanding of current issues and help build relationships between stakeholders and rare disease communities
- Set achievable and clear goals to build momentum, with tangible long-term objectives and measurable milestones



Packaging and Communicating Data

Effectively packaging and communicating data ensures that complex information is accessible and actionable. By presenting data clearly and succinctly, organisations can effectively engage stakeholders, inform decision-making, and highlight the impact of their findings to support advocacy and funding efforts.

How can we communicate data to maximise its impact?

- Use storytelling to make the data relatable and compelling
- Present data visually, with charts and infographics to highlight key messages and themes
- Tailor messages to the specific interests and knowledge levels of different stakeholders
- Ensure transparency by signposting to detailed data sources and methodologies
- Use concise executive summaries to reinforce key messages

Additional Resources

Research Hubs for RWE

Discover-NOW
https://discover-now.co.uk/patients-and-public

The European Health Data & Evidence Network Portal
https://portal.ehden.eu

Clinical Practice Research Datalink (CPRD)
https://www.cprd.com

Drug Repurposing

REMEDi4ALL the European platform for medicines repurposing
https://remedi4all.org

Cures Within Reach providing seed funds for proof-of-concept studies
https://www.cureswithinreach.org

RePo4EU a data hub for information, resources, matchmaking and collaboration
https://repo4.eu

Community and Support

Beacon the rare disease charity for patient groups
https://www.rarebeacon.org

Gene People the genetic conditions support network
https://www.genepeople.org.uk

EURORDIS the European alliance of patient organisations working with rare diseases
https://www.eurordis.org/information-support/find-a-patient-organisation

National Organization for Rare Disorders (NORD) providing resources and training courses
https://rarediseases.org

Genetic Alliance UK a coalition of charities supporting people with genetic and rare conditions
https://geneticalliance.org.uk

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Charity Contact Details

The Chronic Granulomatous Disorder Society

Wayne Kitchener, Trustee

wayne.kitchener@cgdsociety.org

https://cgdsociety.org

SLC6A1 Connect UK-AQ

Lindsay Randall, Founder and CEO

lindsay.randall@slc6a1connectuk-aq.org

https://slc6a1connectuk-aq.org

Timothy Syndrome Alliance (TSA)

Sophie Muir, Founder and Chair

sophie@timothysyndrome.org

https://timothysyndrome.org

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