



Best Data Practices for Rare Disease Patient Foundations and Researchers – PHUSE Working Group Project

Sophia Zilber
December 8, 2023





Introduction

- Leigh syndrome global patient registry – Cure Mito Foundation
- PHUSE working group: [Best Data Practices for Rare Disease Patient Foundations and Researchers](#)
- Patient registry office hours, conferences, podcasts, collaborations (UPenn Orphan Disease Center)



- *"I hope that something comes of this. I have done so many surveys and questionnaires [sic] and NOTHING has ever come of it, NOTHING".*
- *"I am hopeful that I can make useful contributions through my participation that will help others in the future. Otherwise, my participation is in vain. "*
- *"The one thing I wish was to receive the results of the study. Even if the study didn't show how exercise helps delay the onset of HD, it would have been great to at least be shown the results or receive a link to the publication. Letting the patients know about the results is something that all research studies should require. Without the patients, there are no studies!"*



Quotes from patients

Challenges

There's no guidance (from FDA, industry) for registries developed by patient groups.

Many patient groups are fully volunteer or have some staff, but not data analysis/technical knowledge expertise.

Existing guidance documents are for the industry:

Rare Diseases: Natural History Studies for Drug Development Guidance for Industry

<https://www.fda.gov/media/122425/download>



<https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Real+World+Evidence/WP-074.pdf>

Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products Guidance for Industry

<https://www.fda.gov/media/164960/download>



PHUSE working group: best data practices for patient foundations and researchers

PATIENT REGISTRY TRANSPARENCY CHECKLIST FOR PATIENT FOUNDATIONS

INFORMATION TO DISCLOSE ABOUT YOUR REGISTRY PUBLICLY

- ✓ Purpose of the registry
- ✓ Name of the registry vendor
- ✓ What information is collected
- ✓ What medical records collected and how
- ✓ How patient foundation will use the data
- ✓ Frequency and methods of results sharing
- ✓ How can data be accessed
- ✓ Who approves data access
- ✓ Is registry approved by the IRB
- ✓ IRB name and contact information
- ✓ How is data protected
- ✓ Primary contact for the registry

Participants or researchers who are considering working with the registry or donating data are encouraged to ask for these disclosures if they're not provided.

This resource is brought to you by the "Best Data Practices for Rare Disease Patient Foundations and Researchers" Working Group Project



Patient Foundations Guide to Starting a Registry

Know the Purpose of Your Registry

Not all patient registries are the same. Know why you are creating the registry – is it to capture the natural history of the disease, quality of life of patients or caregiver burden, recruit patients for clinical trials, or gather contact information. Assess whether the registry you have in mind is within the scope of what your organization can create. Avoid saying things such as the registry is "to find a cure" as it can introduce false hope.



Involve a Data Advisor from the Start



A data advisor is someone with a technical expertise in clinical data analysis. An appropriate and qualified advisor would provide guidance on selecting patient registry platform, reviewing data dictionary, designing surveys, checking data for completeness and consistency, and analyzing data. Potential educational background to look for: computer science, statistical programming, epidemiology.

Is a Data Dictionary Available?

A data dictionary is a description of the format of the data. It assures the format is one that your foundation can work with. Even if your organization will not do data analysis internally, it is important to understand the data and be able to find information that may be of interest to your community.



Can Raw Data be Exported?



In some cases data is only available within a registry platform without the ability to export it. In this case it is important to understand what virtual environment and tools are available and whether your team has expertise to work within that environment – it is critical to check raw data to make sure it is complete, accurate, and consistent prior to doing analysis.

What Type of Data Do You Plan to Collect?

Know the pros and cons of collecting different data types such as patient-reported data or medical records. If you plan to ask patients to upload medical records, share the purpose of that and know what happens to those records once they're uploaded. Use of validated questionnaires is optimal, however questionnaire should be validated for the specific disease you're collecting data for.



How Do You Plan to Analyze the Data?



Many patient organizations collect data with the hope that it will later be used by researchers, industry, or even regulatory bodies. Unfortunately, this may take a long time or not happen at all, which can be a great disappointment both for the organization and the patients. The most optimal plan is to collect data that your organization can use to raise awareness, share insights, and enable recruitment for clinical trials without depending on external stakeholders.

Governance and Oversight

As with any other project, patient registry requires an appropriate governance framework. Governance may include scientific and medical advisors, legal guidance, ethics oversight, and patient voice. It is important the governance is shared and well known to the registry participants.



IRB



The Institutional Review Board is an organization that oversees the protection of "human subjects" in research. The IRB needs to be consulted when you are planning a registry; it oversees how you consent participants to the registry and all ethical considerations related to communication and data sharing.

Data Privacy

It's important to understand which privacy laws apply for the registry in the local state, federal (USA) or globally, such as the GDPR and the California Consumer Privacy Act. For example, while HIPAA protects data collected by "covered entities," it does not protect data collected by other entities. Understanding these distinctions is important for being transparent with registry participants.



This resource is brought to you by the "Best Data Practices for Rare Disease Patient Foundations and Researchers" Working Group Project



MYTHS VS FACTS ABOUT PATIENT REGISTRIES

We can collect as much data as possible and figure out what to do with it later.



Knowing what you want to do with the data is critical in the beginning. This will determine the type of registry platform you use and the information you will collect.

We should wait for a lot of data to be available before we analyse it.



It's important to start analysing data as soon as you start collecting it to be able to catch errors and fix them early on.

The more data we collect, the better our registry.



More data is not always better. In fact, asking for lots of information may fatigue participants and result in missing or incomplete data. A smaller dataset with only what is necessary is often far more useful.

Using validated instruments is always the best strategy.



While it's important to explore the availability of the validated instruments, if they have not been validated for your disease, they won't necessarily be the best approach.

Doctors and researchers are experts on patient registries.



Doctors and researchers are able to provide input into the type of clinical information that is important to collect as well as help interpret results, but they might not have the technical expertise to run a registry. Relevant backgrounds are data analysis, statistical programming and biostatistics.

We can combine our data with data from other registries.



Combining data can be very challenging unless registries collect data, including data structure, questions, and response options, in the same way. Combining data is time-consuming and requires special expertise, which can be expensive. Therefore, if you want to combine data, it's best to plan for it early on.



This resource is brought to you by the "Best Data Practices for Rare Disease Patient Foundations and Researchers" Working Group Project



ends on many factors, ty of a data dictionary, ards, creating optimal g data analysis, which ly dependent on the cost of the platform.



This resource is brought to you by the "Best Data Practices for Rare Disease Patient Foundations and Researchers" Working Group Project



Common misconceptions about registries among patient groups

Industry, FDA, and researchers would find the data highly valuable

Data can be used as natural history data in a clinical trial (for example as control arm)

Data can be easily combined with any other data or registry can “plug in” to another registry

Data privacy (HIPAA), etc..

UPenn survey - 17/22 responded that patient foundations are required to follow HIPAA

<https://www.orphandiseasecenter.med.upenn.edu/patientregistryfaqs>



MYTHS VS FACTS ABOUT PATIENT REGISTRIES	
We can collect as much data as possible and figure out what to do with it later.	 Knowing what you want to do with the data is critical in the beginning. This will determine the type of registry platform you use and the information you will collect.
We should wait for a lot of data to be available before we analyze it.	 It's important to start analyzing data as soon as you start collecting it to be able to catch errors and fix them early on.
The more data we collect, the better our registry.	 More data is not always better. In fact, asking for lots of information may fatigue participants and result in missing or incomplete data. A smaller dataset with only what is necessary is often far more useful.
Using validated instruments is always the best strategy.	 While it's important to explore the availability of the validated instruments, if they have not been validated for your disease, they won't necessarily be the best approach.
Doctors and researchers are experts on patient registries.	 Doctors and researchers are able to provide input into the type of clinical information that is important to collect as well as help interpret results, but they might not have the technical expertise to run a registry. Relevant backgrounds are data analysis, statistical programming and biostatistics.
We can combine our data with data from other registries.	 Combining data can be very challenging unless registries collect data, including data structure, questions, and response options, in the same way. Combining data is time-consuming and requires special expertise, which can be expensive. Therefore, if you want to combine data, it's best to plan for it early on.
 This resource is brought to you by the "Best Data Practices for Rare Disease Patient Foundations and Researchers" Working Group Project. 	

There's no guarantee that researchers or industry will be interested in the data. Researchers usually need funding in order to work on the data and even then, results may not be available for months or years. Industry may be looking for data that is very high quality or supports a particular drug application.	
There are multiple factors and requirements that may influence regulatory agencies' interest in your data. In the event that a regulatory agency does want to see your data, the best strategy is to have it the best quality possible.	
HIPAA only applies to "covered entities", which includes healthcare providers, health plans and healthcare clearing houses. Most patient registry vendors and patient foundations don't fall into these categories, and therefore HIPAA doesn't apply to their data.	
Besides the technical aspect of data quality, data quality is determined by the accuracy of self-reported data entry and the appropriateness of the questions asked. Both patient-reported and medical records data have limitations.	
There's no clear definition on what "own data" means. Sometimes, patients can consent to how they want their data to be used and can withdraw from participation if they would like. However, the data that has already been extracted from the database may continue to exist. Better definitions of data ownership and clarity on data usage are necessary.	
Data quality depends on many factors, such as availability of a data dictionary, use of data standards, creating optimal surveys and doing data analysis, which are not necessarily dependent on the cost of the platform.	
	

This resource is brought to you by the "Best Data Practices for Rare Disease Patient Foundations and Researchers" Working Group Project.	
--	--

Registry vendor considerations

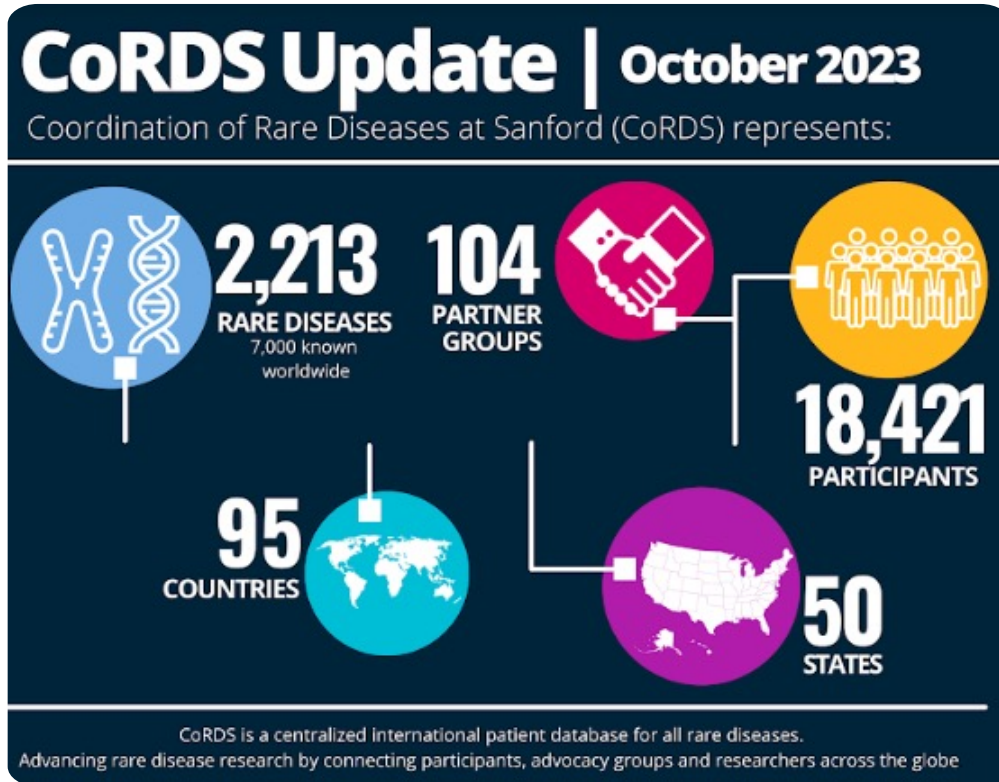
- Price – free vs. paid (price can be per patient, per survey, per question in survey)
- Data access – patient group has access to all of data vs. doesn't have access
- IRB approval – patient group has to submit IRB proposal vs. registry vendor has IRB
- Registry PI – patient group representative is the PI vs. registry vendor representative is a PI
- Data ownership – patient group “owns” data, can move all data to another platform if desired vs. patient group doesn't have this ability
- Data structure, number of surveys that can be created, availability of surveys “built-in”

Patient groups considerations when choosing registry platform

- Common consideration by patient groups: Patient registry vendor has similar values/beliefs about patient advocacy, patient engagement, “Patient owns data”, etc..

Rarely considered by patient groups:

- Data structure
- Raw data availability
- Being able to easily obtain basic information from the data (Example: How many patients have seizures?)
- Ability to share insights and what else they (as an organization) can do with the registry



Leigh syndrome patient registry – Cure Mito foundation

- **Considerations in choosing this platform**
- Easy to contact patients with clinical trial opportunities
- Raw data is available
- Data dictionary is available
- Data structure (NIH common data elements)
- Well designed general survey provided by CoRDS
- Free
- Cure Mito could use data from the very beginning to bring value, regardless if researchers/industry/FDA interest in data

Leigh syndrome patient registry- Cure Mito foundation

Launched by Cure Mito Foundation in September 2021

Partnership with Coordination of Rare Diseases at Sanford (CoRDS) - 100+ patient groups, 2000+ rare diseases

Global registry, ~ 300 participants, 35+ countries

95% - diagnosis genetically confirmed (60% diagnosed within 1 year since symptoms start)

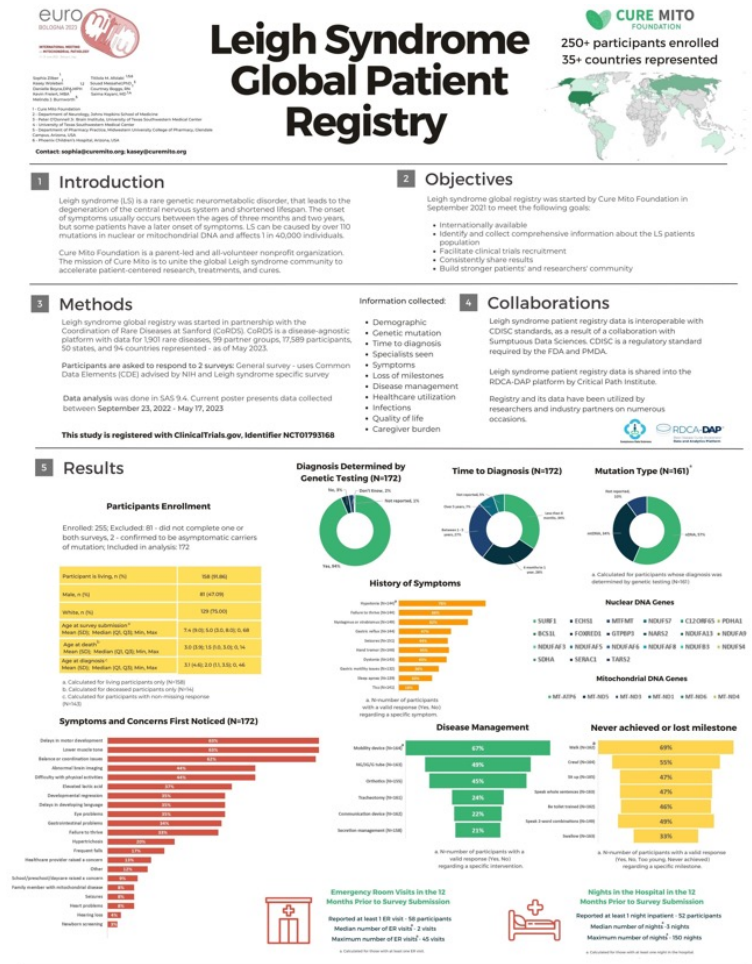
Data is interoperable with CDISC standards (CDASH/SDTM)

Data is shared integrated into RDCA-DAP platform by Critical Path Institute (C-Path)

FDA listening session February 2023

10+ conferences, 4 posters, 2 papers (1 published, 1 in peer review)

Data was shared with researchers, used to share clinical trial opportunities multiple times



Medical records collection

Medical records are collected with patient's consent (Citizen, Picnic Health) mainly to build natural history data to use in clinical trials as a control arm

- Can this data actually be used as a control arm? (vs. prospective natural history study)
- What are other possible uses of such data by industry?
- How does it compare with claims data
 - Implementing standard, consistent, and up-to-date definitions of medical conditions and treatments. These elements employ uniform medical language and are typically provided in advance in study protocols and procedure manuals.
 - Providing a consistent schedule of medical visits for the patient.
 - Providing standard operating procedures for investigators, which provides for greater consistency in the information collected (e.g., using the same clinical outcome assessments with comparable instructions for use).
 - Collecting additional data that may elucidate the pathogenesis and manifestations of a disease and the patient's concomitant treatments.

Source: Rare Diseases: Natural History Studies for Drug Development (FDA guidance)



How data collected by patient groups can help

Make it easy to share
clinical trial
opportunities with
patients

Make data available to
industry and
researchers

Build partnerships
between patient
community and
industry

Understand burden of
the disease

Build strong global
community

Understand patient
and caregiver
perspectives

Thank You!

Email: sophia.Zilber@alexion.com

Connect:

<https://www.linkedin.com/in/sophiazilber/>

The logo for phuse, featuring the word "phuse" in a bold, blue, sans-serif font. The text is centered within a large, light blue circular arc that forms the upper half of a smiley face. The background of the slide is a solid teal color, decorated with abstract white and light blue shapes, including a large white smiley face in the top left and various dotted patterns.