

WITH STANDARDS – UNLOCK THE POWER OF DATA



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Real world data as a bridge between industry and patients

Presented by Sophia Zilber, Rare Disease, Pfizer



Meet the Speaker

Sophia Zilber

Title: Real world data as a bridge between industry and patients

Organization: Pfizer

Sophia Zilber is a Sr. Statistical Programming Lead in Pfizer, where she's managing a team of statistical programmers, preparing the study and asset programming deliverables for submission. She has 20 years of experience with clinical data analysis. Her experience includes programming, creating study documentation, and establishing strategy, timelines, and resourcing of statistical programming and analysis deliverables, following CDISC and regulatory standards.

External to Pfizer, Sophia applies her passion for patient advocacy and data sharing through her involvement with rare disease community. Sophia is currently a board member for Cure Mito Foundation where she's also a patient registry director and has developed a global patient registry for Leigh Syndrome. Sophia has authored papers and has done multiple presentations on the topic of patient registries and data sharing.

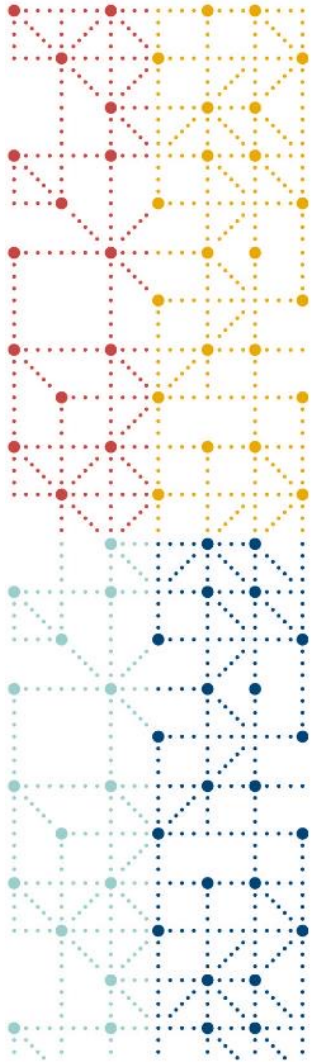
Sophia believes that patients are critical to advancing treatments forward and that sharing knowledge, and open, honest and transparent communication are a key to a successful partnership.





Disclaimer and Disclosures

- *The views expressed in this presentation are the personal views of the author and may not be understood or quoted as being made on behalf of or reflecting the position of the regulatory agency/agencies or organizations with which the author is/are employed/affiliated and do not necessarily reflect the official policy or position of CDISC.*
- *The author(s) have no real or apparent conflicts of interest to report.*



Agenda

1. Background
2. Patients-driven research: advantages, challenges
3. Patient registry for patient reported data – example
4. Aligning patient reported data to CDISC – use case
5. Discussion topics of above example
6. CDISC and Real World Data
7. Opportunities for pharma industry
8. Q&A



Background

Real World Data examples¹:

- Electronic Health Records (EHRs);
- Medical claims and billing data;
- Data from product and disease registries; biobanks;
- Patient-generated data, including from in-home-use settings; and data gathered from other sources that can inform on health status, such as mobile devices



Patient Registries:

- Used to be fully maintained by hospitals or academic institutions
- As patients play a greater role in research, patient registries are frequently run by patients themselves, usually through patient advocacy foundations



Advantages



Patients have a voice in research



Collecting data that's meaningful to patients



Often quicker to collect data, easier outreach



Data can be shared much easier than data collected in other ways (hospital, and other)



Overall faster to advance clinical trials, treatments



Challenges

Quote from patient: *"I hope that something comes of this. I have done so many surveys and questionnaires [sic] and NOTHING has ever come of it, NOTHING"*

Lack of expertise (survey design, data management, data analysis)

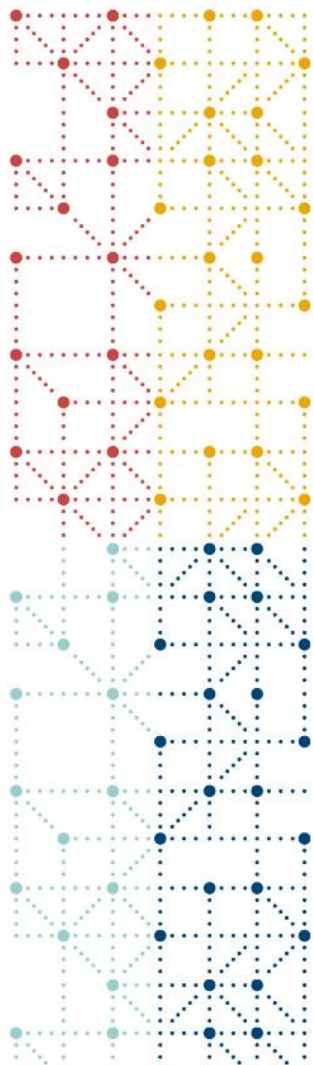
Poor data quality

Data sometimes never analyzed or used

Lack of clarity regarding data privacy and data ownership

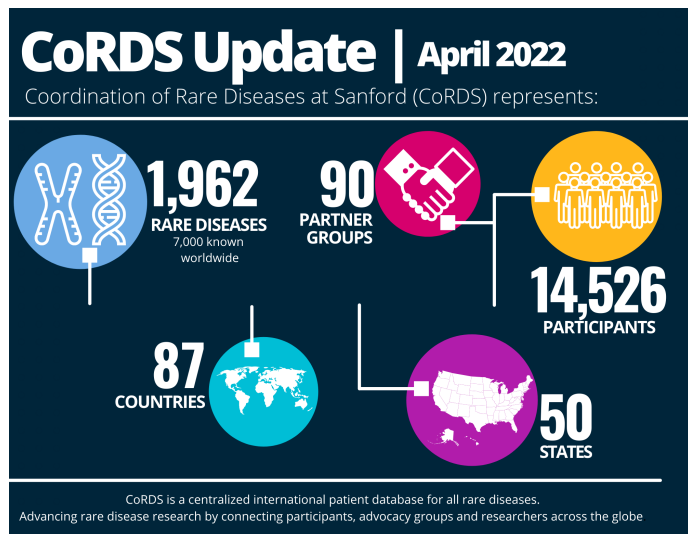
Inaccurate beliefs about data (examples: registry=cure, FDA/industry have high interest in the data, different datasets can be easily combined)

Challenges result in slowing down research, patients discouraged



Patient registry – patient reported data - example

Leigh Syndrome Global Registry – Cure Mito Foundation



Based at Sanford Research, a nonprofit research institution, CoRDS is a centralized international patient registry for all rare diseases.

We coordinate the advancement of research into 7,000 rare diseases. Here's how:

- We work with patient advocacy groups, individuals and researchers.
- We capture health information from individuals with a rare diagnosis, undiagnosed patients, unaffected carriers or at-risk patients.
- We connect researchers and patients and notify our participants of emerging clinical trials.
- We make the registry accessible. Participants can enroll for free and researchers can access it for free.

[Source:https://research.sanfordhealth.org/rare-disease-registry](https://research.sanfordhealth.org/rare-disease-registry)



Leigh Syndrome Global Registry – Cure Mito Foundation

OBJECTIVES

Cure Mito Leigh Syndrome registry was started in September, 2021 to meet the following goals:

- Internationally available
- Identify and collect comprehensive information about LS patients population
- Facilitate clinical trials recruitment
- Share results and findings on an ongoing basis
- Build stronger patients and researchers community



Leigh Syndrome Global Registry – Cure Mito Foundation

General survey – based on NIH survey for rare diseases (Common Data Elements recommended by NIH)

Exactly the same general/demographic survey for each rare disease supported by CoRDS
Easy to harmonize data across rare diseases

Disease specific survey – developed separately for each disease

Linked to Orphanet list of rare diseases

Patient can join even if no advocacy group represented in CoRDS
Joining based on disease

Multiple family members with same disease can be linked together





Leigh Syndrome Global Registry – Cure Mito Foundation

Information collected:

- Diagnosis and genetic mutation information
- Symptoms/concerns first noticed
- Loss of milestones
- Disease management
- Symptoms experienced
- Healthcare utilization
- Quality of life
- Caregiver burden

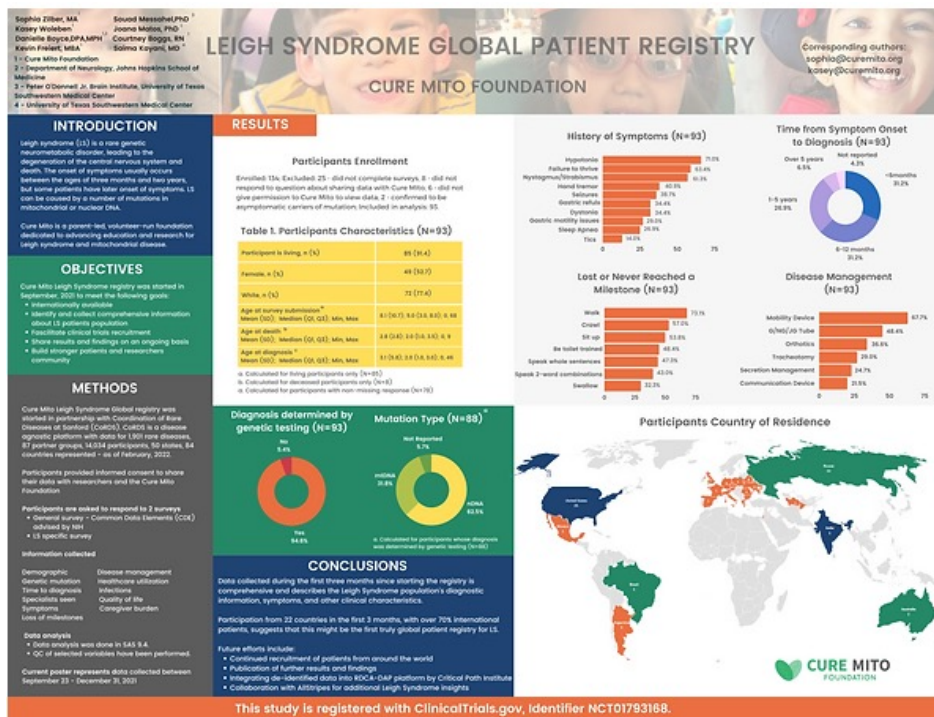




Poster

Mitochondria-Targeted Drug Development Summit, February 22-24, 2022

<https://www.curemito.org/results>



Poster

RESULTS

Participants Enrollment

Enrolled: 134; Excluded: 25 - did not complete surveys, 8 - did not respond to question about sharing data with Cure Mito, 6 - did not give permission to Cure Mito to view data, 2 - confirmed to be asymptomatic carriers of mutation; Included in analysis: 93.

Table 1. Participants Characteristics (N=93)

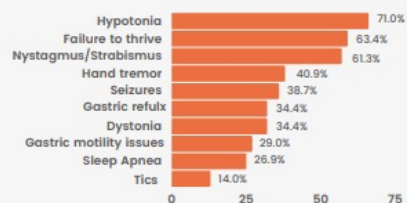
Participant is living, n (%)	85 (91.4)
Female, n (%)	49 (52.7)
White, n (%)	72 (77.4)
Age at survey submission ^a Mean (SD); Median (Q1, Q3); Min, Max	8.1 (10.7); 5.0 (3.0, 8.0); 0, 68
Age at death ^b Mean (SD); Median (Q1, Q3); Min, Max	2.8 (2.8); 2.0 (1.0, 3.5); 0, 9
Age at diagnosis ^c Mean (SD); Median (Q1, Q3); Min, Max	3.1 (5.8); 2.0 (1.0, 3.0); 0, 46

a. Calculated for living participants only (N=85)

b. Calculated for deceased participants only (N=8)

c. Calculated for participants with non-missing response (N=78)

History of Symptoms (N=93)



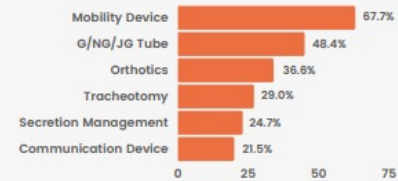
Time from Symptom Onset to Diagnosis (N=93)



Lost or Never Reached a Milestone (N=93)



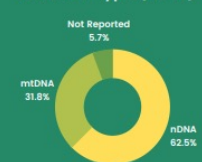
Disease Management (N=93)



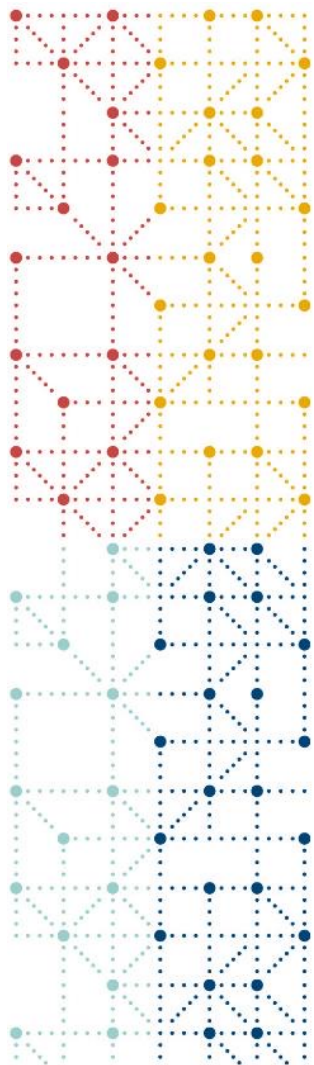
Diagnosis determined by genetic testing (N=93)



Mutation Type (N=88)^a



a. Calculated for participants whose diagnosis was determined by genetic testing (N=88)



Interoperability of Leigh Syndrome Patient Registry Data with Regulatory Submission Standards



Interoperability of Leigh Syndrome Patient Registry Data with Regulatory Submission Standards

- Collaboration with Sumptuous Data Sciences (sumptuous-ds.com)
- CDISC Standards are required for regulatory submissions to FDA (U.S.) and PMDA (Japan) (cdisc.org).
- Goals:
 - Learn if the data is compatible with CDISC
 - Convert data to CDASH and then SDTM
 - Have data that is regulatory submission ready
- Results
 - >90% of data maps to existing CDISC domain
 - Conversion in progress
- Next steps?

PP04

PP04: Alignment and Interoperability of Leigh Syndrome Registry Data with Regulatory Submission Standards
By: Sophia Zilber¹, Pallavi Bakare², Kasey Woleben¹, Saima Kayani^{1,3}, Parag Shiralkar², and Japhanya Bhupathi²

Abstract: The patient data is collected at registries for getting a real-world view of patient reported outcomes, and to know about the diseases more. Establishment of interoperability of registry data with acceptable submission standards like CDISC is essential in order to accelerate the development of therapies and is a critical milestone in case of rare diseases.

This is a pilot project for establishment of such interoperability of patient registry data with CDISC standards. This poster presentation provides an overview of an outcome of this pilot project. The poster provides overview of the current data collection practices of patient registry data collected through validated CDISC patient data registry provides methodological steps executed to convert such data into CDISC requirements and provides further assessment and recommendations pertaining to modification of patient registry data collection instrument.

Background of Patient Registry Data

Leigh Syndrome (LS) is a rare genetic neurodegenerative disorder resulting into degeneration of central nervous system and death. LS can be caused by a number of mutations in mitochondrial or nuclear DNA. Patient registries are particularly important in rare diseases, where patient numbers are small, and funding is limited.

Coordination of Rare Diseases at Sanford (CoRDIS) platform to host the data

NIH Common Data Element Repository (NIH Common Data Element Repository Survey Questionnaire Design)

CoRDIS Patient Registry contains real-world data specific to Leigh Syndrome

Such registry managed data is easily available at the source or collection point.

The data can be used for interaction with regulatory agencies if it is aligned in right standard/formats

Need for Establishment of Interoperability

Establishment of interoperability can help academic, researchers and industry.

- To understand the data for its use for clinical research.
- To analyze and report the data in commonly accepted standards and models.

Approach in Establishing Interoperability of the Data

Step 1: Assessment of NIH data elements	Step 4: Variable alignment with CDASH domain variables
Step 2: Review and assessment of collected data	Step 5: Terminology alignment
Step 3: Alignment of data elements with CDASH Domains	Step 6: Data transformation and compliance assessment

Key Observations

- Patient registry data is a single dataset with all information together. Common data needs to be developed to split the data into domains specific to CDASH (data collection standards of CDISC) requirements.
- Variables need to be differentiated as relevant and irrelevant from clinical significance point of view. Additional variables to be kept from full-survey point of view. Required Data Cleaning
- Horizontal structure of data, needs to be pushed into CDISC required format. Data from single survey form needs to be split into multiple variables.

Current Status:

- Patient registry data is analyzed, and domain map created to split data as per CDASH elements.
- Specific domain of data registry can be mapped to the CDASH domains of AD, CE, CO, DM, DS, PF, IM, and OS - need to map to supplemental domains.
- A lot of data pertaining to Phenomenon/Concepts/Findings, medical history, and Questionnaire domains.
- Programming development of CDASH specific domains in progress.

Next steps:

- Complete the transformation of registry data to CDASH standards and then convert the data to SDTM standards.
- Based on the assessment of the data, and the CDISC specific needs, give feedback to data collection instrument design team for possible design of data elements to adhere to standards.
- By taking CoRDIS/NIH approach convert CDASH based data into SDTM for submission readiness as per USFDA requirements through PDI compliance processes.
- Provide a summary of the process along with compliance assessment to assessment, as well as to industry to foster, promote, and accelerate the data analysis, reporting, and representation practices by a regulatory compliant manner.
- Provide, train, and accelerate the development of novel therapies and treatments to cure Leigh Syndrome.

References:

- 1) Clinical Data Acquisition Standards Harmonization (CDASH) CDASH CDISC
- 2) NIH Common Data Element repository (NIH Common Data Elements CDE) Biobox

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Opportunities for pharma industry

Guidance for patients and patient advocacy groups

- Understanding of drug development process
- Understanding of data and how it's used
- Limitations of data
- Explain data management, data analysis
- Explain value/possible use of patient-reported data, electronic health records

Guidance for researchers

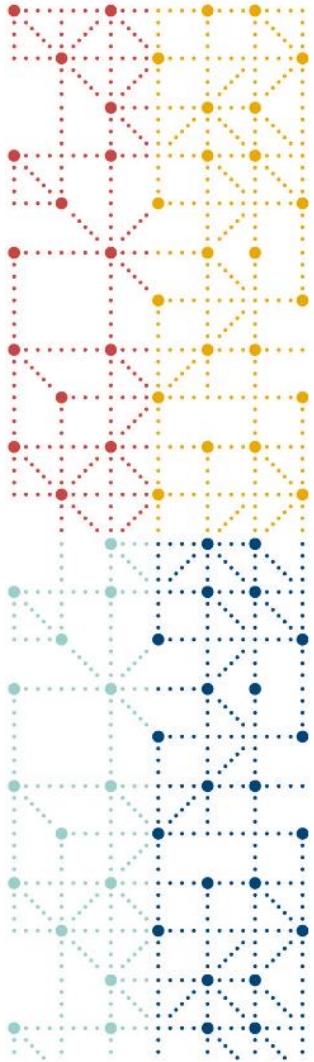
- Explain data from industry perspective
- Explain CDISC
- Value of CDISC standards
- Individual use cases

Why is this important?

- Patients are highly motivated
- A lot of money, time, effort already invested into collecting data
- By identifying and addressing the gaps, we can put patients into the center and get to treatments and cures faster

PHUSE workgroup: Best Data Practices for Rare Disease Patient Foundations and Researchers

<https://advance.phuse.global/display/WEL/Best+Data+Practices+for+Rare+Disease+Patient+Foundations+and+Researchers>



Thank You!

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