Introduction to Odyssey: Real-world rare disease data collection program from digitized health records for patients with long-chain fatty acid oxidation disorders (LC-FAOD) in the United States

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BACKGROUND

Introduction

- LC-FAOD are a group of rare genetic disorders stemming from inborn errors of metabolism[1]
- These chronic diseases present across a broad clinical spectrum, punctuated by episodes of acute, life-threatening metabolic decompensation[1]
- Data are limited for real-world LC-FAOD management and outcomes
- The LC-FAOD Odyssey Program is a central IRB-approved research study from Ultragenyx Pharmaceutical and PicnicHealth, a digital health company, to better understand LC-FAOD
- Odyssey uses a novel patient-centered design to collect prospective and retrospective data on the real-world impact of LC-FAOD, and prospective data of patient- and caregiver-reported outcomes (PROs)

Study Eligibility

- Anyone with an LC-FAOD diagnosis, living in the U.S., and who received care in the U.S. in the past 7 years is eligible to join this study
  - Caregivers can enroll those under the age of 18 years
  - Additional assent is required for participants 7 to 17 years old
- All types of LC-FAOD are eligible, including:
  - CPT I (carnitine palmitoyltransferase I)
  - CACT (carnitine-acylcarnitine translocase)
  - CPT II (carnitine palmitoyltransferase II)
  - VLCAD (very long-chain acyl-CoA dehydrogenase)
  - TFP (trifunctional protein)
  - LCHAD (long-chain 3-hydroxy-acyl-CoA dehydrogenase)

METHODS

- This non-interventional cohort study collects data with the PicnicHealth platform **(Figure 1)** using a novel human-in-the-loop machine learning system to synthesize structured and unstructured data from US medical records **(Figure 2)**:
  - Clinical notes
  - Medications
  - Nutrition records
  - Laboratory and imaging results
  - Diagnostic reports
- Patients complete a survey at enrollment and quarterly for the first year, providing data on:
  - Diagnosis
  - Clinical trial participation
  - Current/previous disease management
  - Symptoms
  - Quality-of-life (measured by EQ-5D-5L)
  - Absenteeism
  - Home management of disease
- Total daily caloric intake (DCI) is calculated for each patient using USDA guidelines[2] for a moderately active person. It was assumed that there were 7.7 kcals/ml and 8.3 kcals/ml for MCT[3] and triheptanoin[4], respectively.
- Patient representatives collaborated on the study design to ensure data relevancy
- Patient data are anonymized, and the study is HIPAA-compliant and IRB-approved
- Results are collected at regular intervals aid study awareness and patient engagement
  - Preliminary results include data from 18 patients
  - Second target: 30+ patients
  - Final target: 100+ patients

Figure 1. PicnicHealth Data Approach

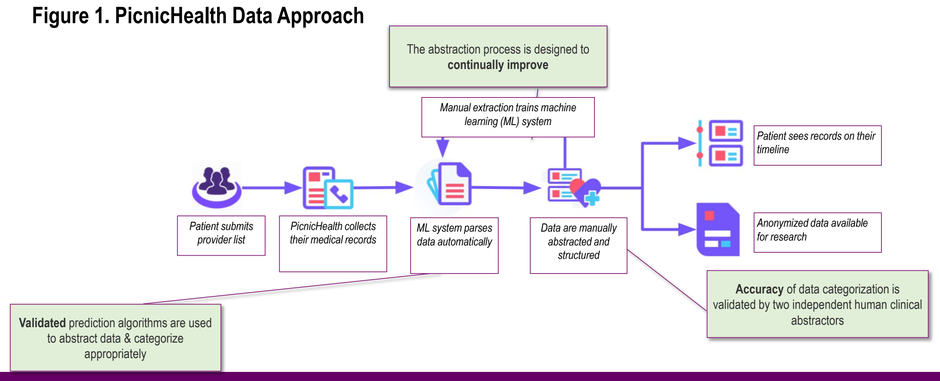
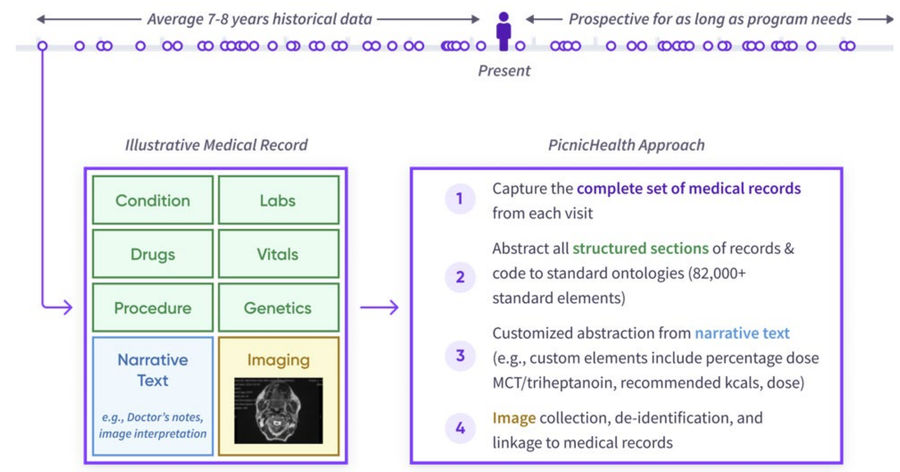


Figure 2. Study Design



OBJECTIVE

- The goal of the LC-FAOD Odyssey study is to collect real-world data from medical records to gain insight into LC-FAOD progression and treatment
- Other objectives of this research include:
  - Centralizing, digitizing, and encrypting medical records for LC-FAOD patients
  - Creating an anonymous, real-world dataset for LC-FAOD researchers to use
  - Understanding treatment patterns and their effectiveness
  - Understanding differences in outcomes

RESULTS

Retrospective Medical Record Data

- 33 patients with LC-FAOD enrolled from August 2020 – August 2021
- Initial retrospective medical records are available for 13 patients (**Table 1**)
  - 38% are female; median age 16 years
  - Median years of retrospective data was 7.5/patient, with median of 15 providers and 6 sites per patient
  - Types of visits and number of visits were captured at patient level across the entire years of data available

Table 1: Retrospective Records Patient Characteristics (N = 13)

Characteristic	N = 13 n (%); Median [IQR]
Sex	
Female	5 (38%)
Male	8 (62%)
Age at Onboarding	16 [8, 23]
Years of Data	7.5 [5.2, 12.4]
Number of Providers	15 [6, 26]
Number of Care Sites	6.0 [3.0, 9.0]
Number of Visits	28 [16, 99]
Number of Outpatient Visits	25 [15, 74]
Number of ER Visits	1.0 [0.0, 8.0]
Number of Hospitalizations	3 [1, 11]
Total Hospital Days	8 [1, 15]
Hospitalizations/Year	0.69 [0.12, 1.07]
Hospitalization Days/Year	0.71 [0.18, 1.85]

ER, emergency room; LC-FAOD, long-chain fatty acid oxidation disorder.

PRO Data

- Of 18 patients with available PROs **(Table 2)**:
  - 50% were female; median age at 18
  - Majority of the patients were LCHAD (n = 9), followed by VLCAD (n = 7)

Table 2: PRO Patient Characteristics (N = 18)

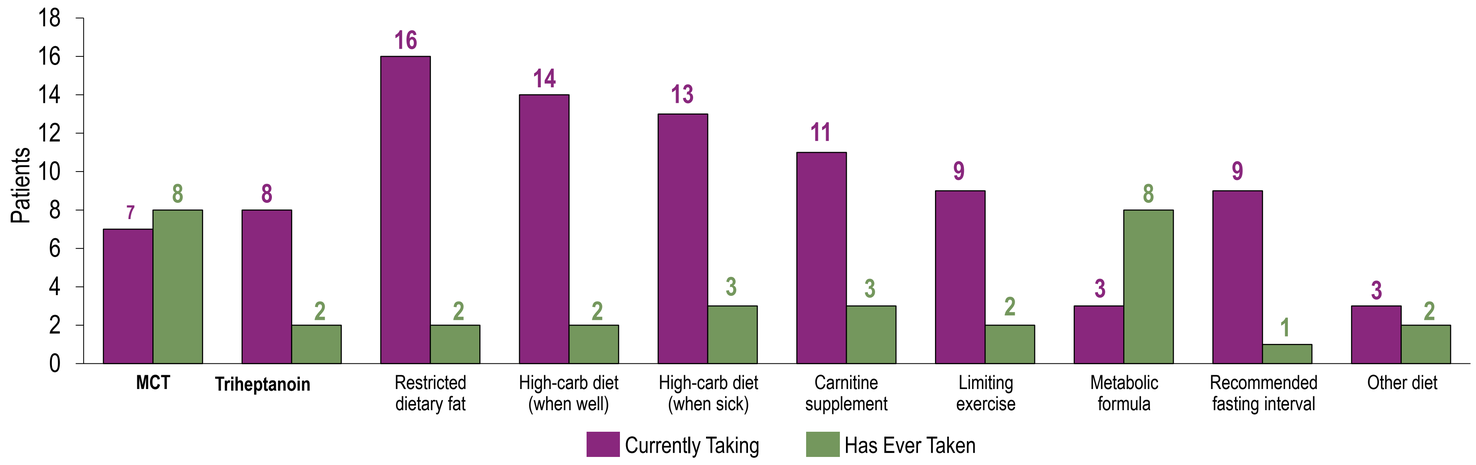
Characteristic	N = 18 n (%)
Sex	
Male	7 (39%)
Female	9 (50%)
Unknown	2 (11%)
Age at Onboarding	18 [12, 28]
LC-FAOD Type	
LCHAD	9 (50%)
VLCAD	7 (39%)
CPTII	1 (6%)
Unknown	1 (6%)

CPTII, carnitine palmitoyltransferase II; IQR, interquartile range; LC-FAOD, long-chain fatty acid oxidation disorder; LCHAD, long-chain 3-hydroxyacyl-CoA dehydrogenase; PRO, patient reported outcome; VLCAD, very long-chain acyl-CoA dehydrogenase.

LC-FAOD Management

- Of 18 patients with PROs, 8 take triheptanoin and 7 take MCT currently **(Figure 3)**

Figure 3: Disease Management Experience (N = 18)



MCT, medium-chain triglyceride; PRO, patient-reported outcome.

Dosing and Fasting

Dosing

- 10 patients reported their MCT and tripheptanoin doses (actual and prescribed doses), which was converted to percentage DCI to enable comparison across ages and treatment
- Average prescribed percentage DCI for MCT patients (n = 4) was 20.5% (range: 8.8%–43.3%) and actual consumption was 17.6% (Range: 8.8%–38.5%).
- Triheptanoin patients (n=6) reported average prescribed and average actual percentage DCI of 27.2% (range: 8.3%–39.4%) and 25.9% (range: 8.3%–39.3%), respectively.

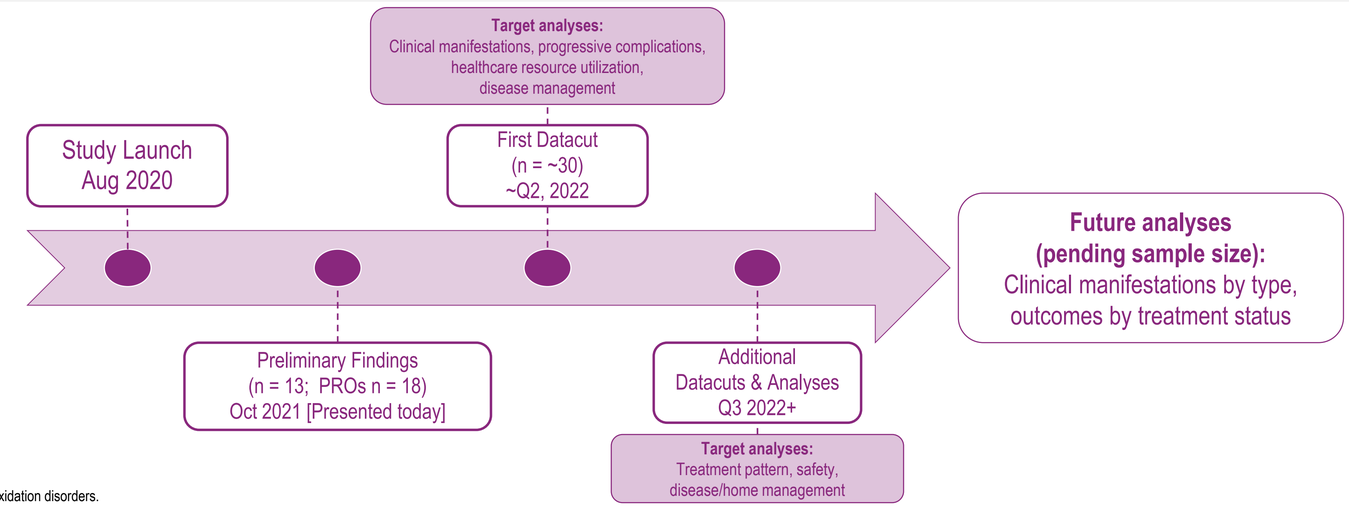
Fasting Intervals

- A total of 10 patients (4 adults) reported their fasting intervals
- Most patients (50%) reported a fasting interval of 8 hours
- The weighted average for all patients' fasting interval was 7.75 hours
  - 8.25 hours for pediatrics (median: 8; range: 4–10)
  - 7 hours for adults (median: 8; range: 4–8)
- Average fasting interval for triheptanoin treated patients (n = 4) and MCT patients (n = 4) were both 7.5 hours (median: 8; range: 4–10)

CONCLUSIONS

- **Preliminary results from Odyssey demonstrates the utility of linking patients' longitudinal medical records and patient reported outcomes:**
  - Data can be extracted across U.S. care providers to derive meaningful data.
  - LC-FAOD care is complex, with multiple providers, care sites, and management strategies.
- **Future real-world LC-FAOD research will investigate journey to diagnosis, burden of illness, disease course and progression, treatment effectiveness, disease management, and unmet patient needs**
- **Additional enrollment will provide a larger-scale real-world dataset for LC-FAOD researchers to use in understanding treatment patterns, their effectiveness, and understanding differences in outcomes.**
  - Greater sample size may enable comparison between types of LC-FAOD
  - Researchers will be able to access anonymized data from LC-FAOD Odyssey through PicnicHealth to further research efforts
  - Published results will be shared directly with patients enrolled in the study

As data continue to mature, Odyssey will advance LC-FAOD research in a multi-phased approach over the next two years



LC-FAOD, long-chain fatty acid oxidation disorders.

DISCLOSURES AND ACKNOWLEDGMENTS

- This study was funded by Ultragenyx Pharmaceutical Inc.
- Medical writing support was provided by Jack Pike, PhD of Ultragenyx Pharmaceutical Inc.
- Eliza Kruger, Erru Yang, Bridget Reineking and Nina Thomas are employees and stockholders of Ultragenyx Pharmaceutical Inc.
- Kieran Mace, Meghan Tierney, Emily Cibelli, Dan Drozd, and Nathan Ross are employees and holders of stock options of PicnicHealth. Dan Drozd holds stock in PicnicHealth.

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Presented virtually at *INFORM 2021;* October 27th and 28th, 2021