

# Symptoms, Treatment Effectiveness and Quality of Life for Patients Living with Long-chain Fatty Acid Oxidation Disorders (LC-FAOD) in the United States: Patient and Caregiver Reported Outcomes from LC-FAOD Odyssey

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## INTRODUCTION

- Long-chain fatty acid oxidation disorders (LC-FAOD) are a group of rare genetic disorders stemming from inborn errors of metabolism<sup>1</sup>
- These chronic diseases present across a broad clinical spectrum, punctuated by episodes of acute, life-threatening metabolic decompensation<sup>1</sup>
- 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 Inc. 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 patient- and caregiver-reported outcomes (PROs) from consenting patients
- The goal of the LC-FAOD Odyssey study is to advance our understanding of LC-FAOD and potentially improve quality of care
- Collected data will be used to assess the real-world impact of LC-FAOD

1. Merritt JL, et al. Rev Endocr Metab Disord. 2020; 21:479-493.

## OBJECTIVE

- Assess patient/caregiver reported management, symptoms and effectiveness of treatment for LC-FAOD and quality of life of people living with LC-FAOD

## 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 for enrollment, 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

- 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 for adults)
  - Home management of disease
- Patient representatives collaborated on the study design to ensure the relevancy of the collected data to patients with LC-FAOD
- Patient data are anonymized, and the study is HIPAA-compliant and IRB-approved
- This analysis includes patients from Odyssey enrolled from August 2020–August 2022

## Patient Demographics and Clinical Characteristics

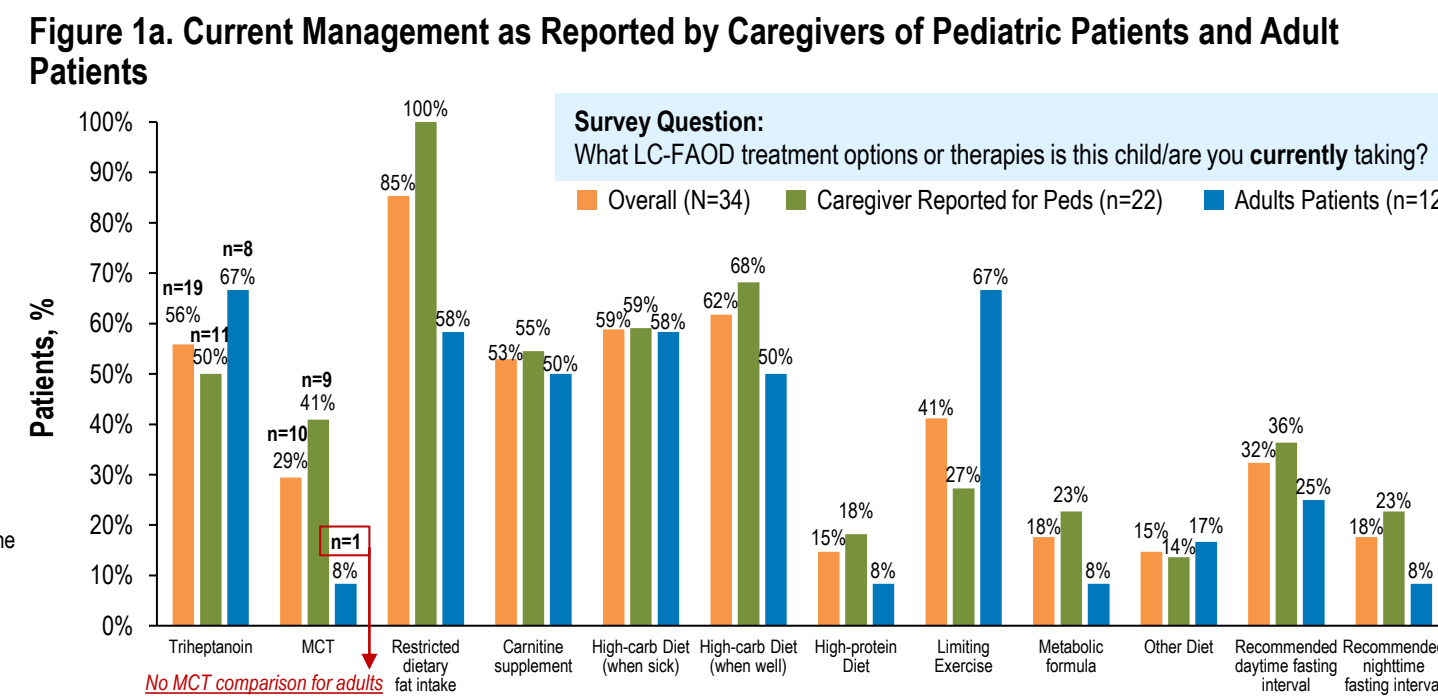
- As of August 2022, 45 patients were enrolled; results from 34 patients (12 adult; 22 caregiver) that completed baseline survey and medical records abstraction were included in this analysis (Table 1)
- Eight of 12 (67%) adult patients were currently on triheptanoin and one (8%) was on MCT
  - Eleven (50%) and nine (41%) of 22 caregivers reported their children were receiving triheptanoin or MCT, respectively

Table 1. Patient Demographics and Clinical Characteristics

Patient Characteristics at Enrollment	N=34	Patient Characteristics at Enrollment	N=34
Sex, n (%)		Number of Care Sites, Median (IQR)	7 (4, 11)
Female	12 (35)	Mean (SD)	8 (4)
Male	22 (65)	Type of LC-FAOD, n (%)	
Race, n (%)		Carnitine palmitoyl transferase (CPT) I deficiency	0
Asian	1 (2.9)	Carnitine palmitoyl transferase (CPT) II deficiency	5 (14.7%)
Prefer not to say	1 (2.9)	Very long chain acyl-CoA dehydrogenase (VLCAD) deficiency	11 (32.4%)
Unknown	1 (2.9)	Long-chain 3-hydroxy-acyl-CoA dehydrogenase (LCHAD) deficiency	15 (44.1%)
White	31 (91)	Trifunctional protein (TFP) deficiency	3 (8.8%)
Ethnicity, n (%)		Carnitine acylcarnitine translocase (CACT)	0
Hispanic or Latino	3 (8.8)	Participation in Clinical Trial or Compassionate Use Program for LC-FAOD <sup>a</sup> , n (%)	17 (50.0%)
Not Hispanic or Latino	24 (71)	UX007-CL201	2 (5.9%)
Prefer not to say	1 (2.9)	UX007-CL202	2 (5.9%)
Unknown	6 (18)	Expanded Access Program/Compassionate Use	5 (14.7%)
Age at Enrollment, Median (IQR)	12 (7, 23)	Dr. Melanie Gillingham's study <sup>b</sup>	5 (14.7%)
Mean (SD)	11.6 (6.7)	Other	3 (8.8%)
Total Years Clinical Data, Median (IQR)	9.1 (6.6, 18.8)	Treatment History <sup>c</sup> , n (%)	
Mean (SD)	11.6 (6.7)	Triheptanoin experience	21 (61.8%)
Number of Providers, Median (IQR)	25 (16, 37)	MCT experience	29 (85.3%)
Mean (SD)	29 (18, 37)		

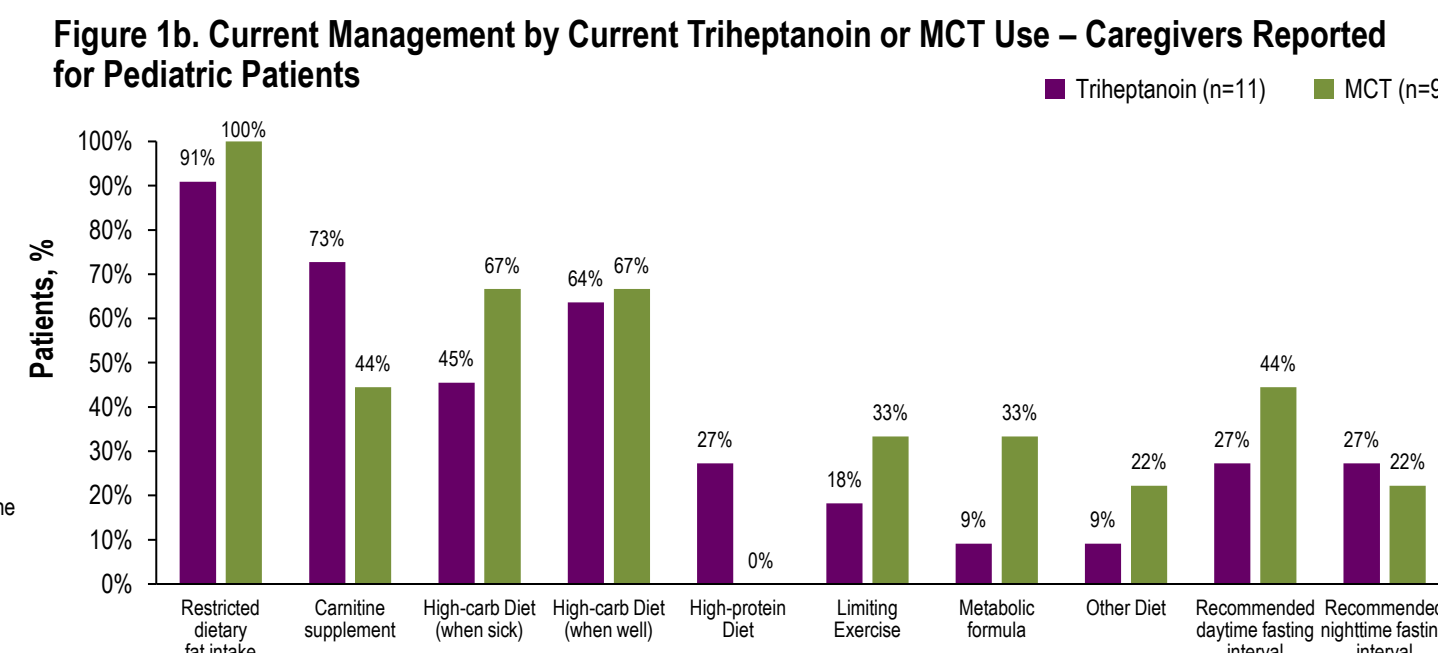
Note: age range (4–44), total years of clinical documents range (1–4–21), number of providers range (3–75), number of care sites range (1–17). <sup>a</sup>From patient/caregiver questionnaire. <sup>b</sup>Gillingham MB et al. J Inher Metab Dis. 2017;40:831-843. <sup>c</sup>Information from study period (with EMR period) only.

- LC-FAOD patients employ multiple disease management strategies concurrently; pediatric and adult patients had different management strategies (Figure 1a)



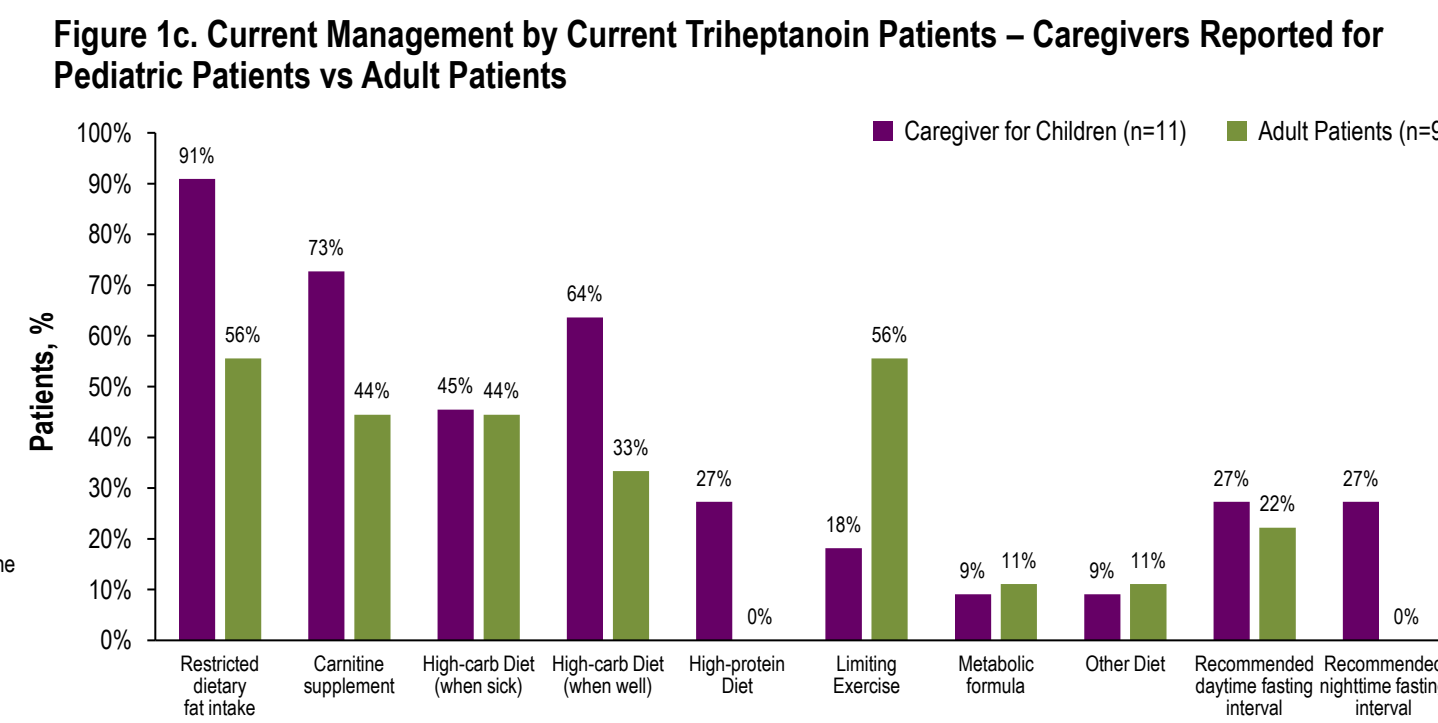
Note: PRO results were reported from baseline survey. LC-FAOD, long-chain fatty acid oxidation disorder; MCT, medium chain triglyceride; PRO, patient-reported outcomes.

- LC-FAOD pediatric patients who are managed with triheptanoin or MCT had different concurrent management strategies reported by their caregivers (Figure 1b)



Note: PRO results were reported from baseline survey. LC-FAOD, long-chain fatty acid oxidation disorder; MCT, medium chain triglyceride; PRO, patient-reported outcomes.

- Pediatric and adult patients who are managed with triheptanoin had different concurrent management strategies (Figure 1c)

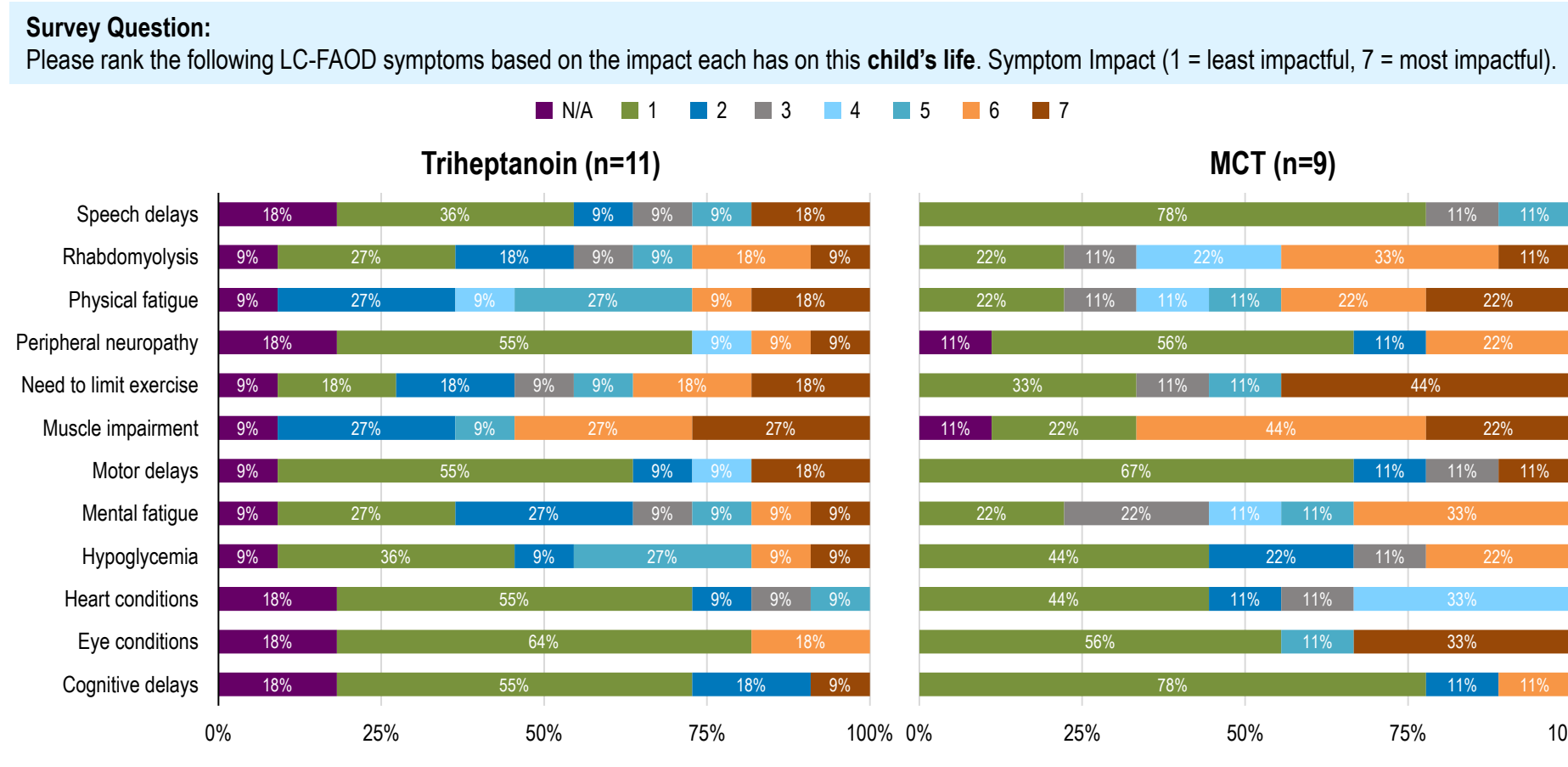


Note: PRO results were reported from baseline survey. LC-FAOD, long-chain fatty acid oxidation disorder; MCT, medium chain triglyceride; PRO, patient-reported outcomes.

## RESULTS

- Muscle/physical function-related symptoms were ranked with highest impact on pediatric patient's life regardless of current treatment (Figure 2a)

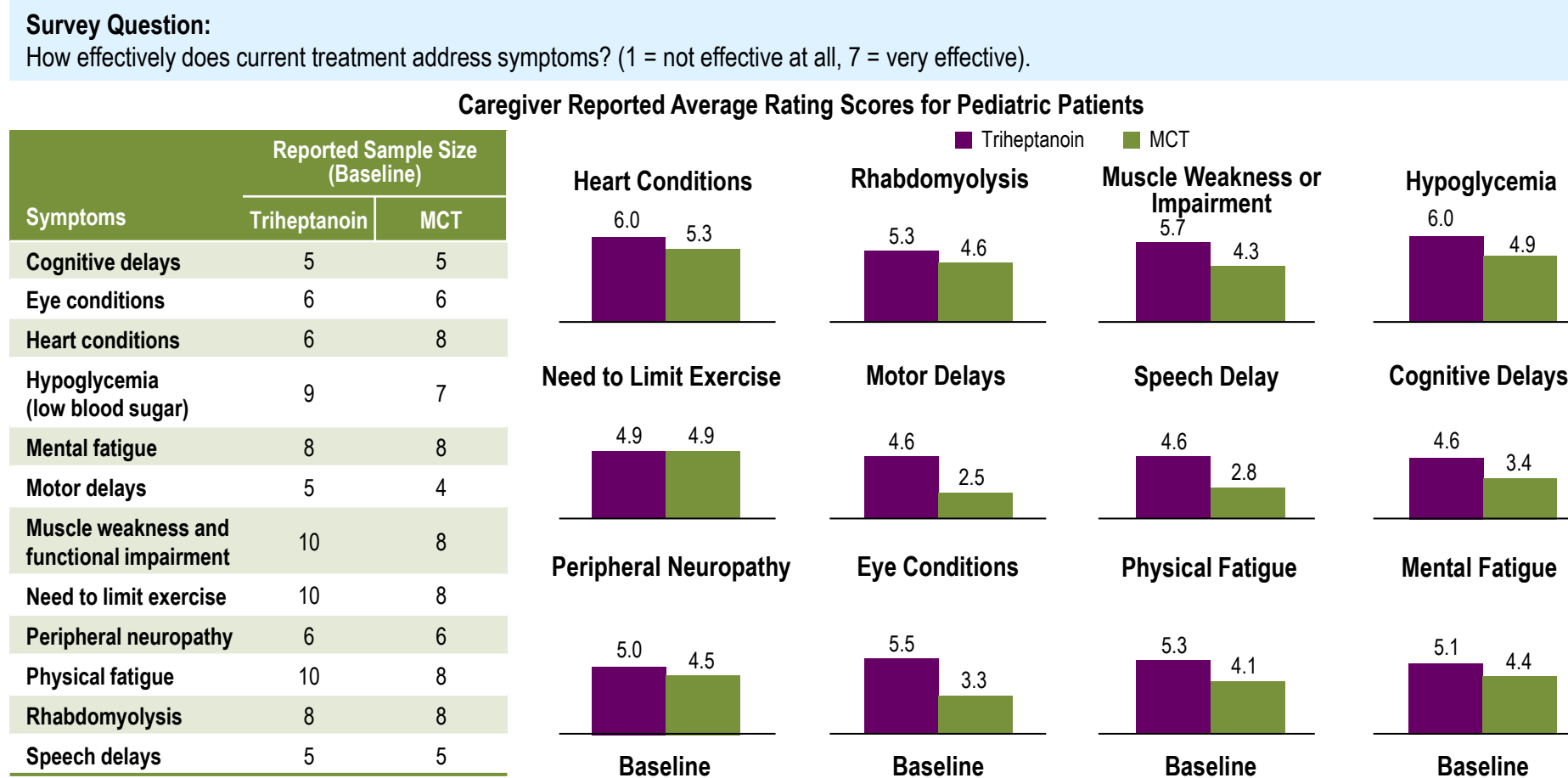
Figure 2a: What Symptoms are Most Impactful? (Pediatric Patients)



Note: PRO results were reported from baseline survey. LC-FAOD, long-chain fatty acid oxidation disorder; MCT, medium chain triglyceride; PRO, patient-reported outcomes.

- Triheptanoin was reported to be more effective in addressing most symptoms versus MCT among pediatric patients (Figure 3a)

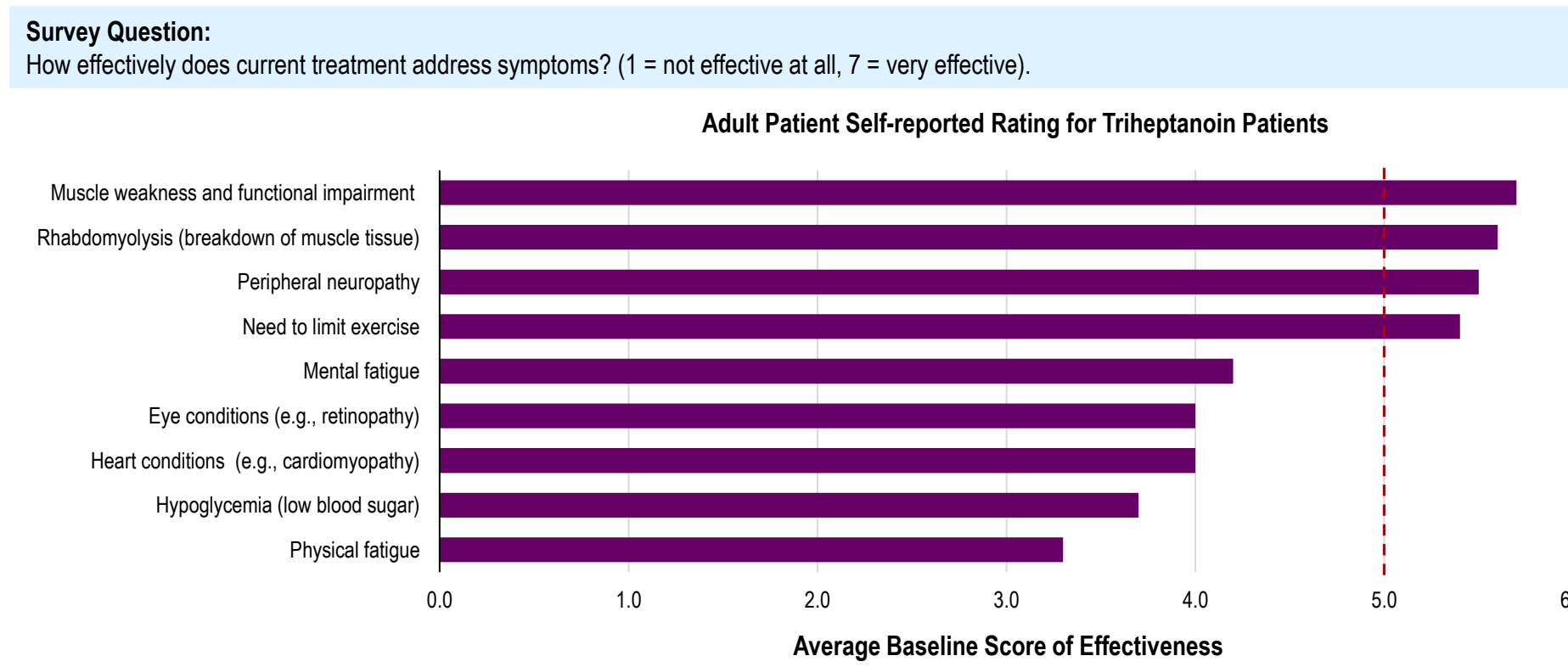
Figure 3a. Efficacy of Triheptanoin in Treating Symptoms in Pediatric Patients



Note: results in follow-up surveys had consistent trend but with small sample sizes. LC-FAOD, long-chain fatty acid oxidation disorder; MCT, medium chain triglyceride; PRO, patient-reported outcomes.

- Triheptanoin was reported to be most effective in addressing muscle functions, physical fatigue and need to limit exercise in adults (Figure 3b)

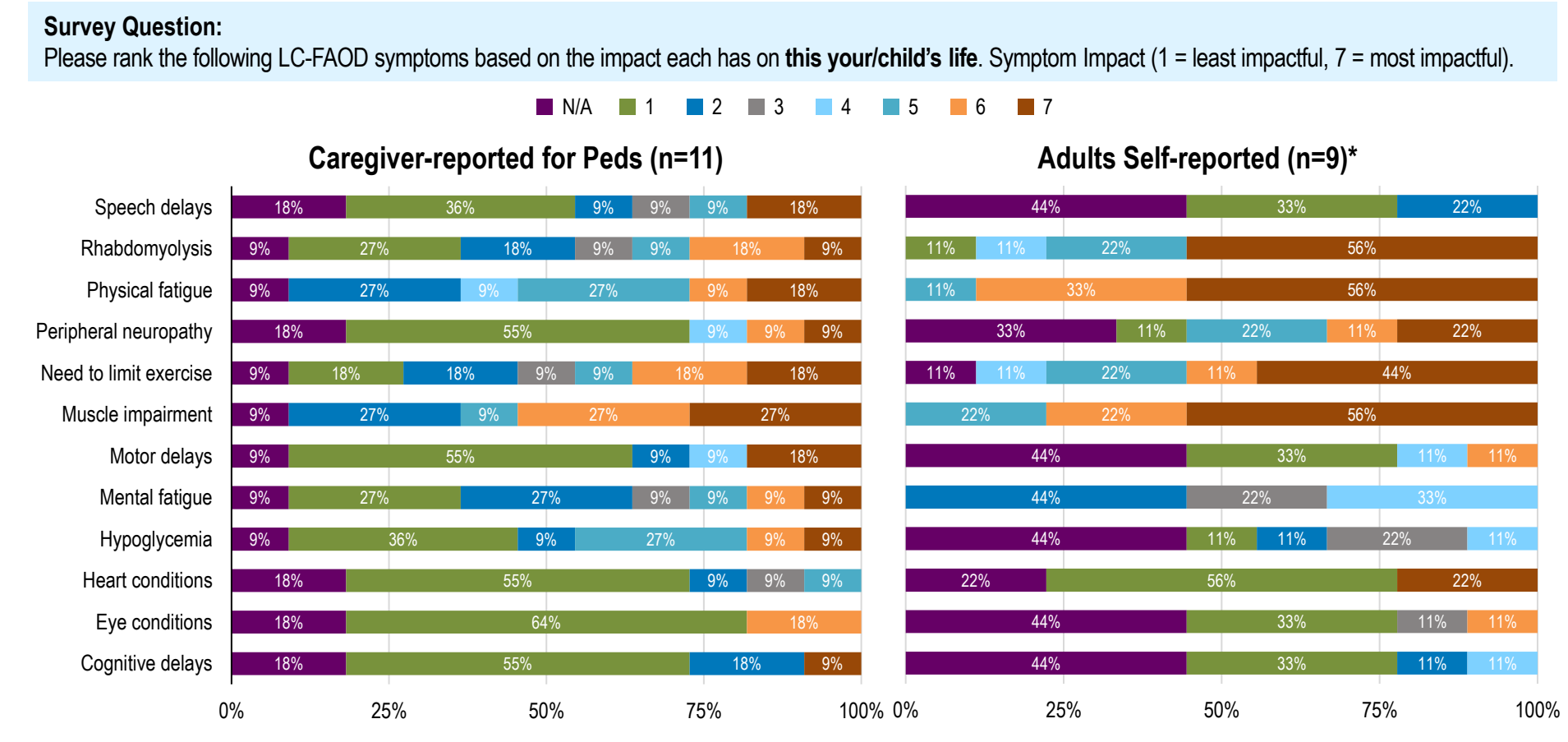
Figure 3b. Efficacy of Triheptanoin in Treating Symptoms in Pediatric Patients



LC-FAOD, long-chain fatty acid oxidation disorder; MCT, medium chain triglyceride; PRO, patient-reported outcomes.

- Adult patients ranked higher impact of muscle impairment, rhabdomyolysis, physical fatigue and need to limit exercise but lower impact of hypoglycemia (Figure 2b)
- Muscle impairments, need to limit exercise, physical fatigue, and rhabdomyolysis were ranked with highest impact on the lives of patients regardless of treatment or age, with greater impact reported by adults

Figure 2b: What Symptoms are Most Impactful? (Patients Currently Treated with Triheptanoin)



Note: PRO results were reported from baseline survey. \*No MCT comparison due to small sample size in MCT group. LC-FAOD, long-chain fatty acid oxidation disorder; MCT, medium chain triglyceride; PRO, patient-reported outcomes.

- Adult patients treated with triheptanoin reported improved quality of life after treatment, mostly driven by better mobility and daily activities (Figure 4; Table 2)

Figure 4: Quality of Life (EQ-5D-5L) Reported by Triheptanoin Adult Patients

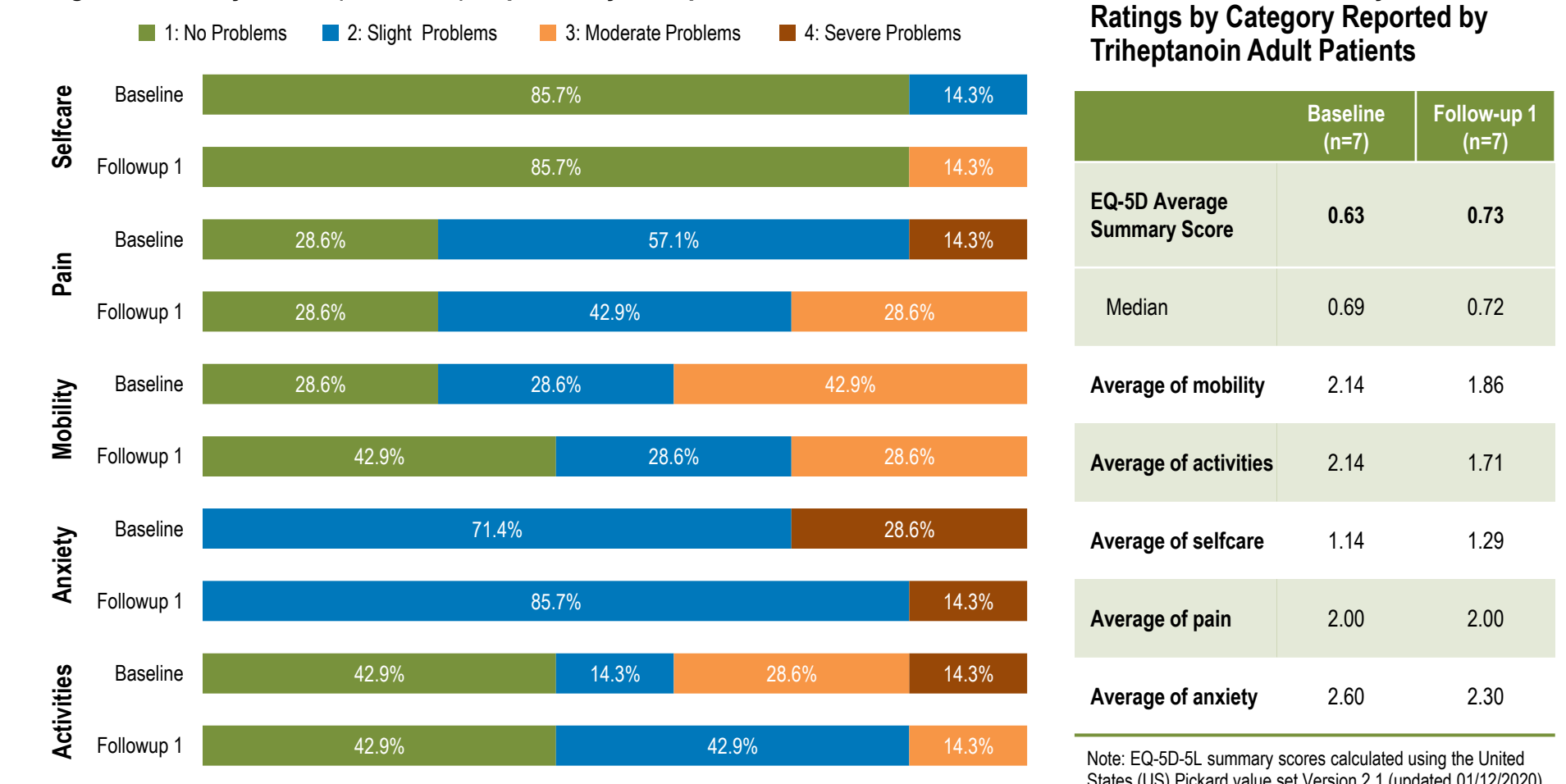


Table 2: EQ-5D Summary Scores and Ratings by Category Reported by Triheptanoin Adult Patients

	Baseline (n=7)	Follow-up 1 (n=7)
EQ-5D Average Summary Score	0.63	0.73
Median	0.69	0.72
Average of mobility	2.14	1.86
Average of activities	2.14	1.71
Average of selfcare	1.14	1.29
Average of pain	2.00	2.00
Average of anxiety	2.60	2.30

Note: EQ-5D-5L summary scores calculated using the United States (US) Pickard value set Version 2.1 (updated 01/12/2020).

## LIMITATIONS

- Real-world evidence is not standardized; there can be significant variance across the cohort
- Any patient with LC-FAOD could sign up for this study; therefore, the population could be much more diverse versus patient populations from clinical trials with restrictive eligibility criteria
- PRO data collected directly from patients/caregivers can be subject to biases (e.g., recall)
- Limited sample size for study cohorts, especially for number of patients currently receiving MCT

## CONCLUSIONS

- PRO data indicated patients with LC-FAOD employ multiple disease management strategies; the management strategies were different for pediatric vs adult patients
- Physical function related symptoms mostly impact LC-FAOD patients' lives, especially among adults
- Caregivers of pediatric patients reported that Triheptanoin was more effective in addressing most symptoms surveyed versus MCT
- For adult patients with LC-FAOD, Triheptanoin was reported to be effective in addressing physical functioning related symptoms and improved quality of life in physical functioning domains

## DISCLOSURES AND ACKNOWLEDGEMENTS

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