Introduction to Odyssey: Real-world Rare Disease Data Collection Program from Digitized Health Records of Patients with Glycogen Storage Disease Type III (GSDIII) in the United States

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INTRODUCTION & OBJECTIVE

- GSDIII is a rare inherited deficiency of glycogen-debranching enzyme that leads to liver, heart, and skeletal muscle damage[1,2]
- Real-world data regarding GSDIII management and patient outcomes are limited
- The GSD Odyssey research study is designed to:[3]
  - Better understand GSDIa and GSDIII progression, how it is managed in the real world, and what needs are still faced by the community
  - Centralize medical records to help patients access and organize their medical records, better manage their care, and contribute their anonymized data to research
  - Construct an anonymous, comprehensive GSDIa and GSDIII dataset that can be used by academic researchers
  - Better understand how GSDIII is experienced in the real world to improve how GSDIII research is conducted moving forward
- GSD Odyssey is currently enrolling both adults and children who are living with GSDIa or GSDIII in the US and can be used by patients/caregivers to better manage their care
- The objective of this study is to report preliminary results from patients with GSDIII who are enrolled in GSD Odyssey

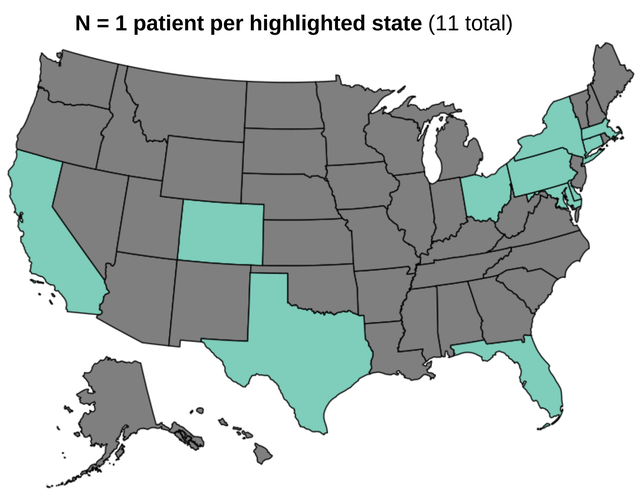
METHODS

- Non-interventional cohort study (target: 30+ GSDIII patients) that collects prospective and retrospective data with the PicnicHealth digital record platform using a novel human-in-the-loop machine learning system to structure US medical records (clinical notes, medications, laboratory/imaging results, diagnostic reports)
- The study is HIPAA-compliant and IRB-approved; all patients or caregivers of patients <18 years provided written informed consent; and data are anonymized
- Records are assessed for any mentions of specific complications or assistive devices and mentions of specific diets or nutrition management within the prior 3 years to indicate recent disease management

US Patient Living With GSDIII	PicnicHealth Digital Record Platform	Researchers
Electronically authorize PicnicHealth to collect their medical records; patients or caregivers can sign up on behalf of patients	Requests and collects medical records from all providers a patient has seen	Receive completely de-identified, research-ready dataset
Sign consent form electronically; minors aged 7-17 are also asked for their assent	Transforms records into the Patient Medical Records Timeline	
Electronically enter treating healthcare professionals and associated facilities	Extracts, structures, and de-identifies data	Utilize dataset to advance understanding of GSDIII and answer key research questions

RESULTS

Figure 1. Eleven patients with GSDIII were enrolled from December 2020 through May 2022.



- Mean age at enrollment was 45 years (range, 7–57)
- More than half of patients (55%) were female
- Median years of retrospective data was 6.1 per patient, with 24 providers and 5 care sites per patient

Table 1. The most common manifestations of GSDIII were fatty liver, hepatomegaly, rhabdomyolysis, weakness, and hypoglycemia.

Category	Complication	Patients n (%)
Cardiovascular	Cardiomyopathy	4 (36%)
Hepatic	Fatty liver	10 (91%)
	Hepatomegaly	9 (82%)
	Liver fibrosis	2 (18%)
	Cirrhosis	1 (9%)
	Liver transplant	1 (9%)
Musculoskeletal	Rhabdomyolysis	6 (55%)
	Myopathy	5 (45%)
	Myalgia	3 (27%)
	Osteoporosis	1 (9%)
Other	Weakness	10 (91%)
	Hypoglycemia	7 (64%)
	Gastrostomy	3 (27%)

Table 2. The most common GSD-related procedures were urine ketone tests and DEXA scans.

Procedure	Patients n (%)
Urine ketone test	10 (91%)
Bone density (DEXA) scan	5 (46%)
Blood ketone test	4 (36%)
Feeding tube placement	3 (27%)
Gastrostomy placement	3 (27%)
Continuous glucose monitoring	2 (18%)
Fracture-related surgeries	2 (18%)
Liver biopsy	2 (18%)
Endoscopy (hepatic-related)	1 (9%)
Liver transplant	1 (9%)
Heart transplant	0 (0)

Table 3. Wheelchairs, walkers, and canes were used by over a third of patients in the study.

Device	Patients n (%)
Use ever observed	
Wheelchair	6 (55%)
Walker	5 (46%)
Cane	4 (36%)
Crutch	3 (27%)
Scooter	2 (18%)
Orthotic device	0 (0%)

Table 4. The majority of patients were on a high-protein diet and/or received cornstarch therapy.

Category	Management	Patients n (%)
Diet (ever* in last 3 years)	High-protein	8 (73%)
	Carbohydrate restricted	5 (46%)
	High-carbohydrate	1 (9%)
	Low-sugar	1 (9%)
	Ketogenic	0 (0%)
Nutrition management (ever* in last 3 years)	Cornstarch	6 (55%)
	Glycosade starch	3 (27%)
	CGM	2 (18%)
	Feeding tube	1 (9%)

*Patients were deemed on a diet type based on narrative mentions in their medical record.

Figure 2. A variety of valuable, de-identified data are abstracted from real-world records over many years and settings.

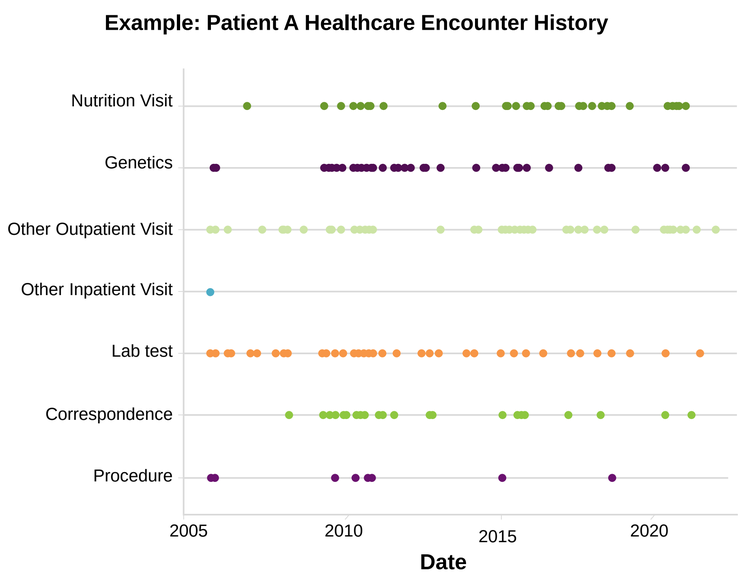


Figure 3. Key lab values were also observed over time for patients as part of Odyssey.

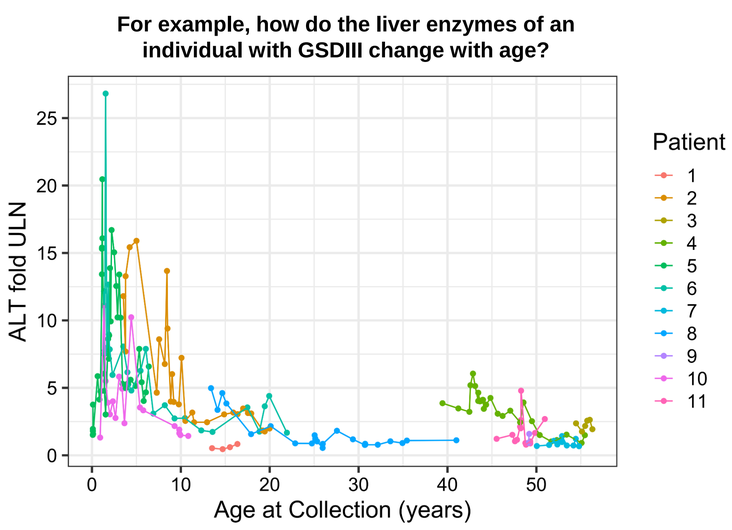
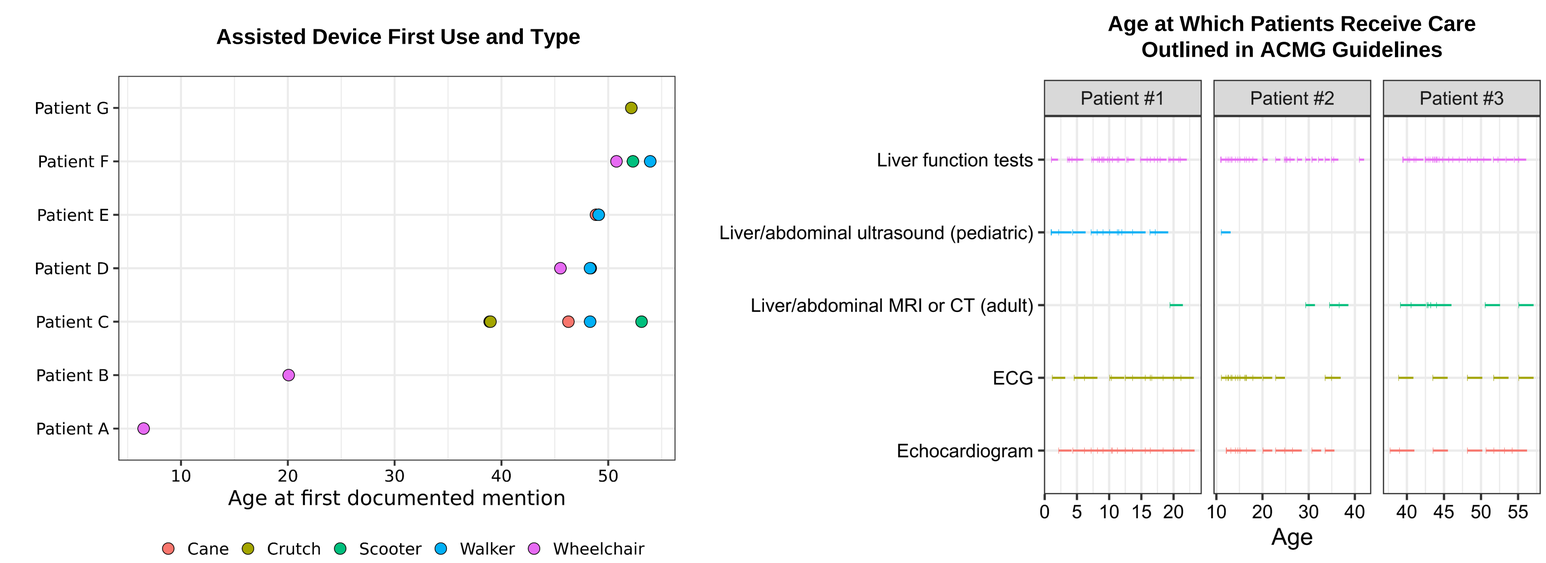


Figure 4. Disease complications and surveillance needs change as patients grow and develop.



CONCLUSIONS & NEXT STEPS

- Meaningful data can be extracted across the US healthcare system using this novel machine learning method, which is already providing insight to guide clinical development of a new therapy for GSDIII
  - More robust data are expected with additional patient enrollment
- **Future questions to address with Odyssey data:**
  - How do disease markers change over time? How frequently are patients hospitalized/visiting the ER? What is the burden of current standard of care?
- **Future applications of Odyssey data:**
  - Continued contribution to the body of literature on GSDIa and GSDIII; Eventual support of regulatory submissions for investigational drugs
- **We are still enrolling adults and children who have received medical care in the US**

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DISCLOSURES

DRB: Receives research support from Ultragenyx and Moderna for GSD related projects; HS: Receives research support from Ultragenyx and is a consultant for Moderna; EK, RNG, NAT, AAG: Employees, shareholders of Ultragenyx Pharmaceutical Inc.; MT, JRD: Employees of PicnicHealth. This study was funded by Ultragenyx Pharmaceutical Inc. Medical writing support was provided by Michelle Kelly, PhD of Ultragenyx Pharmaceutical Inc.