

Treatment patterns and cost of care among patients with Metachromatic Leukodystrophy (MLD) in the US: results from a US claims data analysis

Ali Mohajer¹, Francis Pang², Karen Bean², Christopher Fields²
¹Qral Group LLC, Great Neck NY, US; ²Orchard Therapeutics, London, United Kingdom and Boston MA, US

RWD57

Background & Objectives

Background

- MLD is an ultra-rare (~1:100,000 newborns) neurodegenerative genetic disease caused by deficiency of the lysosomal enzyme arylsulfatase A (ARSA) and resulting in a build-up of toxic sulfatides. This leads to motor and cognitive decline and premature death.^{1, 2}
- MLD phenotype is classified according to age of onset as late infantile (LI ≤ 2.5), early juvenile (2.5 < EJ ≤ 6), late juvenile (6 < LJ ≤ 16), and adult (A > 16). There is evidence to suggest that early-onset phenotypes (LI and EJ) comprise a contiguous disease entity.³
- The prognosis for patients without treatment is very poor, particularly in early-onset MLD. The median time from symptom onset to loss of all voluntary movement with only head control remaining has been reported as 1.12 years for LI MLD and 2.7 years for EJ MLD.⁴
- Prior to premature death, the disease is associated with considerable clinical, psychosocial, and economic burden. The burden of disease of early onset MLD is rated amongst the highest of all debilitating genetic conditions.^{5, 6}

Objective:

The objective of this study was to understand treatment patterns, healthcare resource utilization, and costs of care among patients with early-onset MLD in the US.

Methods

Data Sources

- Full longitudinal medical and prescription claims data from Symphony PatientSource for 1,710 patients having at least one ICD-10 E75.25 diagnosis Jul 2018 - Aug 2022. Data timeframe: Jul 2013 – Aug 2022.

Inclusion criteria

- Patients are required to have received leukodystrophy diagnoses on at least two distinct service dates, at least one of which is ICD-10 E75.25. Patient birth year must be 2014 or later.

Phenotype assignment

- Age of MLD onset is defined here as the age at which the first leukodystrophy diagnosis (ICD9 330.0 or ICD10 E75.25) is observed in claims data. Since patient age granularity is birth year, phenotype assignments are as follows: LI: 0-2; EJ: 3-6; LJ: 7-8. Inclusion criteria and the data timeframe guarantee that age of onset is no more than 8.

Care-category assignment

- Care category is determined using ICD / CPT coding in claims data.

Cost calculation

- Cost per procedure / drug dispensing is derived directly from approved final adjudicated medical and prescription claims data. Capture rates are as follows:
 - i. Procedure cost (to payer): > 99.8%
 - ii. Prescription out-of-pocket cost (to patient) > 99.1%
 - iii. Prescription plan payment (from payer) > 76.7%
- A total of 40.2K procedure and 30.6K prescription claims were examined for 248 eligible patients over the data timeframe.

Table 1: MLD average annual cost of care – all phenotypes

Average annual cost of care		By year relative to MLD onset																By quartile (\$)				Share of quartile				
		Index - 8	Index - 7	Index - 6	Index - 5	Index - 4	Index - 3	Index - 2	Index - 1	Index	Index + 1	Index + 2	Index + 3	Index + 4	Index + 5	Index + 6	Index + 7	Index + 8	Q4	Q3	Q2	Q1	Q4	Q3	Q2	Q1
Category																										
Nursing care in the home		\$0	\$0	\$0	\$0	\$36	\$2,431	\$4,604	\$4,500	\$7,613	\$14,815	\$19,699	\$26,249	\$29,290	\$19,708	\$27,700	\$24,118	\$0	\$39,063	\$423	\$409	\$29	43%	2%	4%	1%
Enteral and parenteral therapy		\$0	\$0	\$1,072	\$1,929	\$2,101	\$710	\$1,402	\$2,163	\$4,943	\$7,291	\$7,128	\$10,567	\$15,296	\$18,601	\$16,227	\$12,925	\$3,275	\$12,251	\$5,210	\$1,822	\$528	13%	25%	19%	15%
Evaluation and management		\$515	\$571	\$2,801	\$1,943	\$1,688	\$4,847	\$1,963	\$2,276	\$5,425	\$4,870	\$3,375	\$2,805	\$1,655	\$2,969	\$2,094	\$1,335	\$877	\$8,417	\$2,917	\$1,401	\$737	9%	14%	14%	22%
Other medical procedures and services		\$766	\$613	\$789	\$566	\$1,843	\$1,766	\$1,431	\$1,891	\$5,080	\$4,764	\$4,531	\$5,647	\$4,801	\$4,653	\$3,789	\$2,952	\$0	\$7,244	\$3,436	\$1,429	\$612	8%	16%	15%	18%
Durable medical equipment		\$0	\$0	\$0	\$22	\$241	\$365	\$452	\$471	\$2,502	\$4,199	\$4,034	\$3,752	\$3,815	\$6,083	\$5,529	\$11,169	\$3,895	\$5,415	\$1,804	\$1,153	\$159	6%	9%	12%	5%
Prescription drugs		\$20	\$16	\$56	\$147	\$74	\$1,052	\$1,660	\$1,116	\$1,001	\$2,710	\$3,842	\$4,978	\$2,552	\$3,170	\$1,848	\$149	\$0	\$5,046	\$1,093	\$532	\$380	6%	5%	5%	11%
Surgery		\$0	\$15	\$810	\$244	\$234	\$1,036	\$820	\$659	\$1,981	\$1,825	\$2,161	\$2,131	\$2,012	\$392	\$0	\$0	\$0	\$2,948	\$1,378	\$682	\$46	3%	7%	7%	1%
Pathology and laboratory		\$0	\$14	\$1,086	\$570	\$522	\$478	\$474	\$1,031	\$1,912	\$1,411	\$1,127	\$786	\$676	\$383	\$1,149	\$3,202	\$0	\$2,373	\$993	\$304	\$313	3%	5%	3%	9%
Other services in the home		\$0	\$0	\$0	\$0	\$0	\$313	\$2	\$3	\$1,301	\$1,788	\$900	\$806	\$853	\$3,352	\$6,357	\$14,569	\$17,460	\$1,955	\$882	\$474	\$111	2%	4%	5%	3%
Transportation		\$0	\$0	\$225	\$203	\$9	\$105	\$201	\$234	\$944	\$1,542	\$1,731	\$963	\$804	\$1,385	\$775	\$1,112	\$382	\$2,444	\$556	\$252	\$26	3%	3%	3%	1%
Radiology		\$19	\$5	\$719	\$323	\$469	\$402	\$349	\$931	\$1,691	\$830	\$792	\$781	\$289	\$498	\$248	\$263	\$0	\$1,520	\$1,135	\$454	\$157	2%	5%	5%	5%
Administered parenteral drugs		\$0	\$0	\$39	\$61	\$14	\$29	\$50	\$46	\$487	\$1,032	\$1,463	\$1,706	\$677	\$1	\$0	\$0	\$0	\$1,432	\$359	\$33	\$21	2%	2%	0%	1%
Orthotics and prosthetics		\$0	\$0	\$0	\$101	\$430	\$211	\$53	\$372	\$563	\$658	\$631	\$768	\$650	\$704	\$1,382	\$0	\$0	\$675	\$448	\$410	\$150	1%	2%	4%	4%
Anesthesiology		\$0	\$0	\$340	\$199	\$369	\$367	\$323	\$347	\$910	\$306	\$189	\$254	\$97	\$19	\$0	\$0	\$0	\$814	\$360	\$327	\$147	1%	2%	3%	4%
Totals		\$1,319	\$1,233	\$7,937	\$6,308	\$8,031	\$14,111	\$13,783	\$16,042	\$36,355	\$48,039	\$51,605	\$62,193	\$63,469	\$61,918	\$67,098	\$71,794	\$25,889	\$91,596	\$20,993	\$9,680	\$3,417	73%	17%	8%	3%
Patient count		2	8	12	18	42	91	145	194	247	211	152	90	59	26	13	7	2	62	62	62	62	62	62	62	62

Figure 1: Cost distribution over year-of-life relative to MLD onset by phenotype

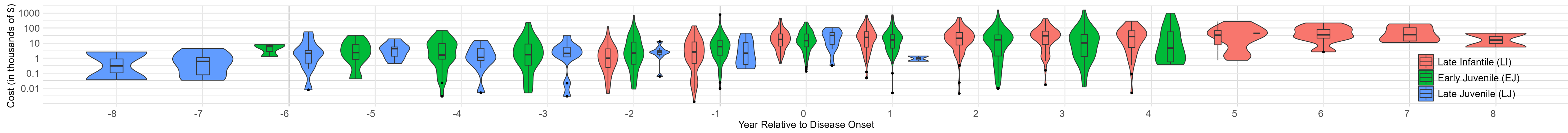


Figure 2: Service cost analysis: total cost by category / MLD onset type; patient-year adjusted category cost

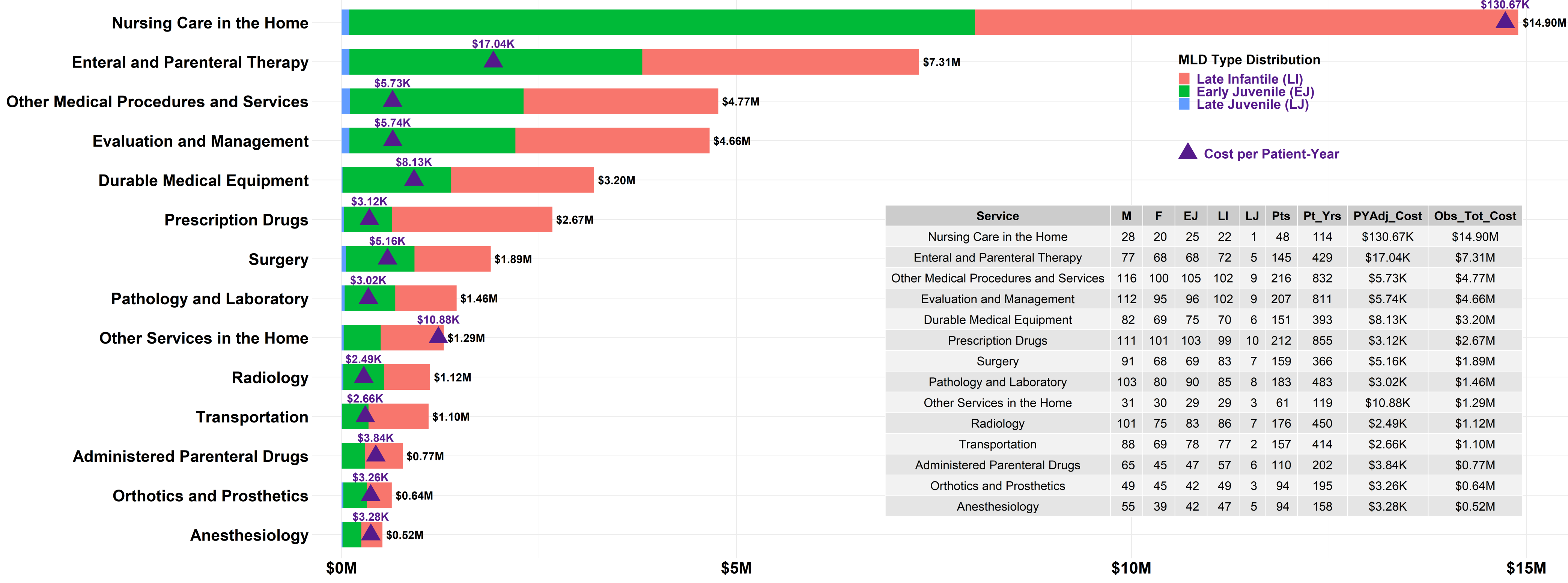


Figure 3: Age-of-onset sample demographics

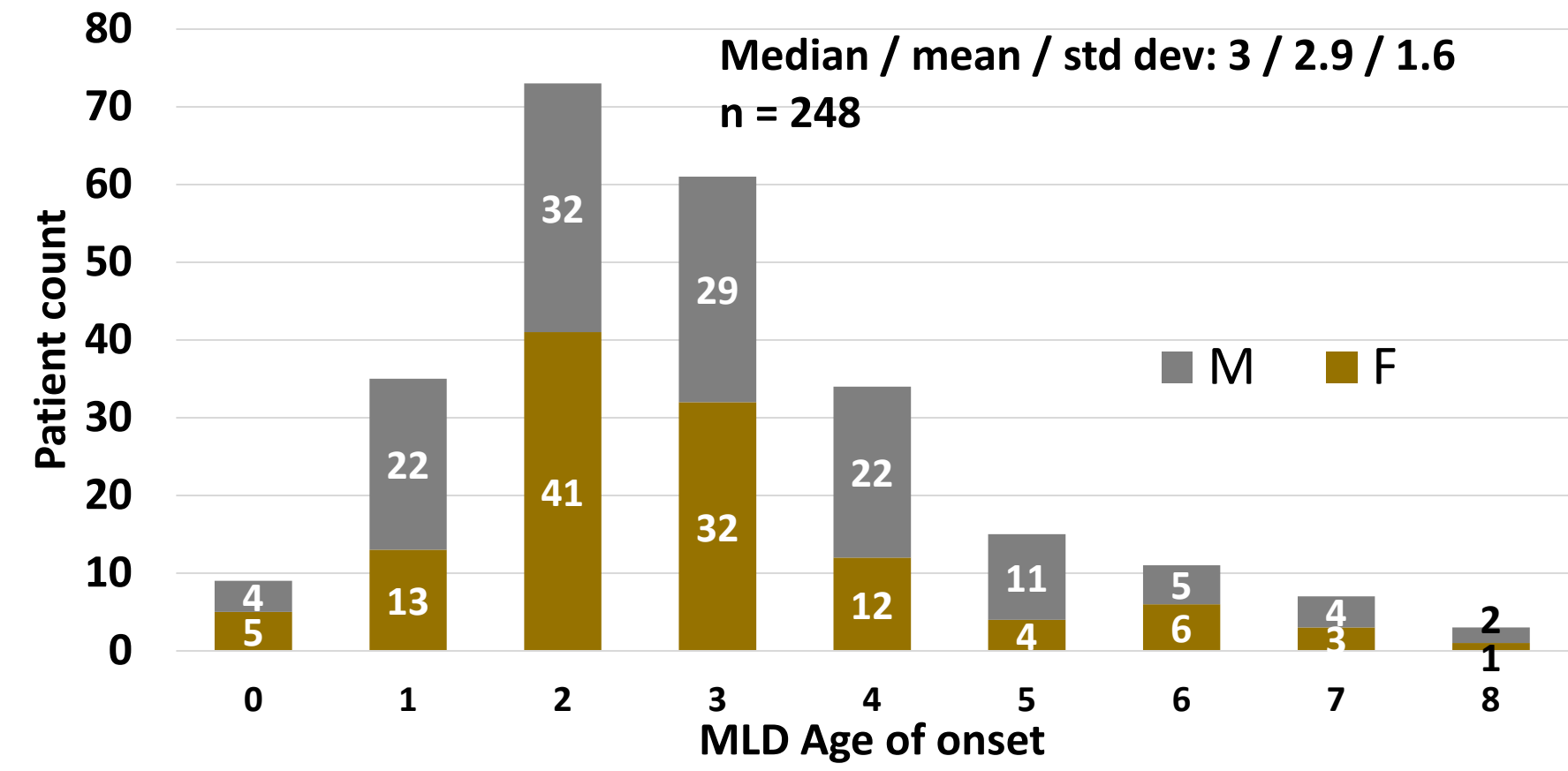
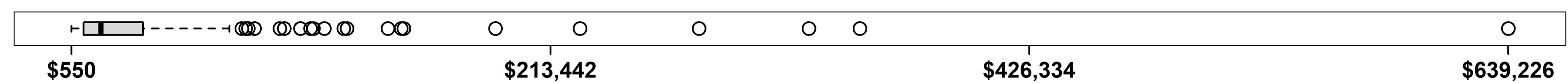


Table 2: Average annual cost sample demographics

Onset type	LI	EJ	LJ
Demographic			
Mean annual cost	\$35,547	\$29,289	\$8,989
Patient count	117	121	10
Male / Female	58 / 59	67 / 54	6 / 4

Results

- A total of 248 MLD patients were identified; 117 were classified as LI onset (58M/59F), 121 as EJ (67M/54F), and 10 as LJ (6M/4F). The mean (SD) and median age of MLD diagnosis was 2.9 (± 1.6) years and 3 years, respectively. No significant evidence of dependence between gender and phenotype is observed (p-value: 0.64 from Fisher's Exact Test). [Table 2; Figure 3]
- Average annual cost of care is heavily skewed, with the top quartile mean over 26x larger than that of the bottom quartile (Pearson median / Bowley skewness: +6.01 / +0.41). Nursing care in the home is the key driver of this disparity [Table 1].



- Average annual cost of MLD care increases sharply in the year of diagnosis and is positively correlated with disease progression. Weighted least-squares (WLS) regression shows highly significant positive correlation (R^2 : 0.80; F-stat: 28.78; DF: 1, 7; p-val. 0.001), predicting average annual cost at \$39.7K (p-val. $< 10^{-6}$) in the year of diagnosis, increasing by \$5.6K (p-val. 0.001) per year thereafter.
- Stratification by phenotype (WLS regression with interaction) suggests statistically significant (p-val. 0.01) differences between the LI and EJ subtypes. LI onset is associated with higher cost at index while EJ onset is associated with steeper increase. (LI: \$43.9K + \$3.3K/yr. vs EJ: \$31.7K + \$13.0K/yr.)
- Prior to MLD diagnosis, evaluation and management is a top cost driver. Post-diagnosis, home nursing care is highest [Table 1]. We find the predicted home nursing cost at MLD index year to be \$10.2K, increasing by \$3.8K per year thereafter (WLS: R^2 : 0.71; F-stat: 17.27; DF: 1, 7; p-val. < 0.01). Stratification by phenotype shows that this effect is most visible in the EJ subtype.

Discussion & Conclusion

- This analysis of claims data provides a comprehensive view of cost of MLD care across top-level categories according to disease progression and constitutes a lower bound estimate of absolute health-system costs. Home care (e.g., nursing, nutrition) constitutes the highest overall cost driver, both in absolute terms and in terms of patient-year adjusted cost.
- Cost are calculated based on available claims data, which is subject to censoring and is likely an underestimate. Certain cost categories (e.g., caregiver lost income, home modifications, travel) are examined elsewhere and not included in this analysis.
- The brief life-expectancy associated with the LI phenotype and the coarse time-granularity and date-masking of birth-year medical claims data suggest that focused investigation of the EJ subtype in future claims analyses may enhance the quality of findings, particularly for predictive analytics.

Conclusion

This analysis is the first study to investigate the relationship between costs and disease progression for MLD using claims data. It provides real-world evidence that MLD cost of care increases with disease progression and categorizes and quantifies the significant cost borne by MLD patients and the health system to obtain a diagnosis and to access specialized care.

References

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Disclosures

- AM is an employee of Qral Group, LLC, which received payment from Orchard Therapeutics for the development of this study.
- FP, KB and CF are employees of and hold stock and/or option in Orchard therapeutics.