Cost of pediatric liver transplant among commercial and Medicaid insured patients

Tamir Miloh,[1] Andrea Goldstein,[2] Robin Howard,[2] Jessica R Marden,[3] Katherine Gaburo,[3] Philip Rosenthal[4]

[1]Department of Pediatrics, Pediatric Transplant Hepatology, Miami Transplant Institute and University of Miami, Miami, FL, USA; [2]Mirum Pharmaceuticals, Inc., Foster City, CA, USA; [3]Analysis Group, Inc., Boston, MA, USA; [4]Department of Pediatrics, Division of Pediatric Gastroenterology, Hepatology, and Nutrition, University of California San Francisco (UCSF), San Francisco, CA, USA

1946

Introduction

- Pediatric liver transplant (LT) is associated with significant healthcare resource utilization (HRU), including inpatient and outpatient medical visits, and cost burden. Previous estimates suggest that pediatric LT cost over $270 million US dollars ($) a year (based on data from 2004, converted to equivalent amount for 2019).[1]
- LT is an effective approach for a range of pediatric liver diseases; however, it can result in a number of complications, leading to significant morbidity and mortality (estimated 5-year mortality rate of 11.6%).[2,3]
  - Post-transplant immunosuppression increases the risk of infections and malignant complications,[4–6] and can result in significant costs, particularly when accounting for the prolonged survival of children post-LT, who may require immunosuppression throughout their lives.[7,8]
  - Graft rejection, which is more common in children, is also associated with additional costs and HRU burden due to liver biopsies and hospital admissions.[9]
  - Moreover, an estimated 8–29% of patients who receive an LT will require re-transplantation, which has higher morbidity and mortality rates.[10–12]
- Between 2011 and 2021, 5,741 LTs were performed in children in the United States,[13] with the majority of patients with cholestatic liver disease requiring a transplant before they reach adulthood.[14–17]

Aim

- To estimate the economic burden associated with pediatric LT among patients with cholestatic liver disease, by evaluating the HRU and total cost of pediatric LT in commercially-insured and Medicaid-insured populations in the United States, using insurance claims data.

Methods

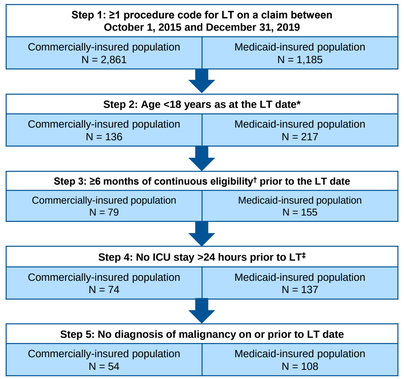
Data sources and cohort selection

- Health insurance claims data from October 1, 2015 to December 31, 2019 from the IBM® Watson Health MarketScan® Commercial Claims and Encounters and Multi-State Medicaid databases were analyzed retrospectively.
  - The children in this analysis are drawn from a subset of the US population with available claims data in the database.
  - Children receiving an LT aged <18 years, with an LT claim between October 1, 2015 and December 31, 2019, and ≥6 months of continuous eligibility prior to the LT date, were included.
- An algorithm was developed with input from clinical experts and validated using data from the United Network for Organ Sharing (UNOS), and the following criteria were used to exclude status 1A or 1B patients including patients with other severe liver conditions like viral hepatitis (**Figure 1**):
  - No ICU stay beginning >24 hours prior to and including index LT, in order to specifically exclude status 1A patients;
  - Diagnosis of any malignancy (hepatic or extra-hepatic) on or prior to LT date.
- Patients were followed until the earliest of: death; or end of follow-up, for up to 5 years post-LT date. The study period started 90 days before the LT date, and the baseline period was defined as 6 months prior to the LT date.

Study outcomes

- All-cause HRU and costs were assessed throughout the study period.
- All-cause costs were defined as the total costs reimbursed by insurers, based on claims data, and reported in 2019 US dollars ($).
- The HRU categories assessed included: all visits, outpatient visits, home care visits, inpatient visits, emergency department visits, and other visits.
  - Home care visits were defined as any visit with a home healthcare provider.
  - Other visits were defined as visits associated with durable medical equipment or dental and vision care.
- HRU and costs were reported as annualized rates, which were calculated by dividing each patient's total values by their study period duration.
- In order to understand how HRU and cost burden may fluctuate in the 3 months before and the 12 months following transplant, an exploratory analysis of HRU and costs across 3-month time periods was conducted for the subset of children who received an LT with ≥12 months of continuous eligibility after the index LT.
  - Values were reported as the average total number of visits and average total costs per patient over each 3-month period.

Figure 1. Identification of children who underwent LT.



*The LT date was defined as the earliest occurrence of a procedure code for LT.
†Continuous eligibility was defined as continuous enrollment in commercial or Medicaid insurance plans and continuous prescription drug coverage.
‡This step was taken to exclude status 1A patients; however all PICU stays >24 hours were excluded.
ICU, intensive care unit; LT, liver transplant.

Results

Patient characteristics

- This analysis included 54 commercially-insured and 108 Medicaid-insured children who underwent LT.
- Baseline characteristics for the commercially-insured and Medicaid-insured populations are shown in **Table 1**.

Table 1. Baseline characteristics for commercially-insured and Medicaid-insured populations.

Patient characteristics	Commercially-insured population (N = 54)	Medicaid-insured population (N = 108)
Demographic characteristics at LT date		
Age, mean (± SD)	7.0 (± 6.0)	5.9 (± 5.4)
Age categories		
≥0 to <2 years	20 (37.0)	43 (39.8)
≥2 to <6 years	6 (11.1)	21 (19.4)
≥6 to <10 years	7 (13.0)	17 (15.7)
≥10 to <18 years	21 (38.9)	27 (25.1)
Male	23 (42.6)	55 (50.9)
Clinical characteristics during the baseline period (6 months pre-transplant)*		
ICD-10 diagnoses linked to LT claim†		
Cirrhosis	41 (75.9)	66 (61.1)
Hypertension	4 (7.4)	13 (12)
Portal hypertension	32 (59.3)	51 (47.2)
Pruritus	8 (14.8)	29 (26.9)
Renal diseases	2 (3.7)	10 (9.3)
Failure to thrive	18 (33.3)	25 (23.1)
Nutritional deficiencies or malnutrition	32 (59.3)	61 (56.5)
Congenital heart disease	15 (27.8)	30 (27.8)
Bone fractures	3 (5.6)	6 (5.6)
Congenital malformation and deformations of the musculoskeletal system and spine	4 (7.4)	8 (7.4)
Rickets	15 (27.8)	43 (39.8)
Procedures associated with cholestatic liver diseases†		
Biliary surgery, including surgical biliary diversion, HPE and other biliary surgeries	2 (3.7)	7 (6.5)

All values are n (%) unless otherwise specified.
*Selected characteristics that were reported in ≥5% of the population.
†International Classification of Diseases, Tenth Revision (ICD-10) Clinical Modification codes were used to identify relevant diagnoses and ICD-10 Procedure Coding System and Current Procedural Terminology codes were used to identify relevant procedures.
LT, liver transplant; HPE, hepatoportoenterostomy; SD, standard deviation.

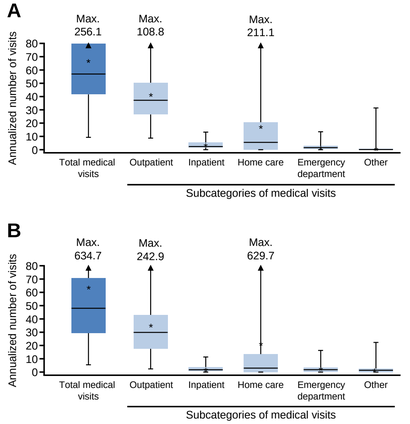
All-cause HRU

- The mean study period duration was 1.7 years (range 0.3–3.9) for the commercially-insured population and 1.8 years (range 0.3–4.0) among the Medicaid-insured population.
- During this period, commercially-insured patients experienced an annualized mean of 67.8 medical visits (range 9.5–256.1), and Medicaid-insured patients experienced a mean of 63.5 medical visits (range 5.5–634.7) (**Figure 2**).
  - Outpatient visits accounted for the majority of the total number of medical visits.
- Commercially-insured patients experienced an annualized mean of 3.5 inpatient visits per year (range 0.0–13.3), with a mean total duration of inpatient stay of 36.7 days per year (range 0.0–139.5).
- Medicaid-insured patients experienced an annualized mean of 2.6 inpatient visits per year (range 0.0–11.1), with a mean total duration of inpatient stay of 35.5 days per year (range 0.0–281.2).
- The majority of commercially-insured and Medicaid-insured patients experienced ≥1 emergency department visit per year.

HRU and costs across 3-month time periods

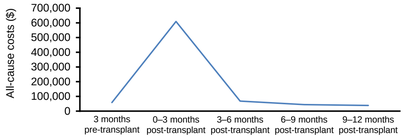
- In the 32 commercially-insured patients eligible for the sub-analysis, the total number of medical visits was greatest in the 3- to 6-month period post-transplant (mean 19.7; range 1.0–79.0), but there were also a substantial number of medical visits 6–12 months post-transplant (0–3 months mean [range]: 16.0 [2.0–67.0]; 6–9 months: 13.3 [1.0–41.0]; 9–12 months: 12.9 [0.0–28.0]).
  - The largest driver of total medical visits during each time period was outpatient visits.
- In the 65 Medicaid-insured patients eligible for the sub-analysis, medical visits were highest in the 3 months immediately post-transplant (mean 20.4; range 1.0–282.0), which was largely driven by outpatient visits. This population also experienced a substantial number of healthcare visits in the 6–12 months post-transplant (3–6 months mean [range]: 17.1 [0.0–222.0]; 6–9 months: 12.4 [0.0–134.0]; 9–12 months: 13.0 [0.0–113.0]).
- Total medical costs were highest in the 0–3 month period (which included LT costs) for the commercially-insured and Medicaid-insured populations, with mean costs of $609,100 (range $1,208–$2,052,575; **Figure 3**), and $223,064 (range $0–$768,590; **Figure 4**), respectively.
- Patients incurred costs throughout the first year post-transplant in both populations (3–6 months mean [range]: $67,890 [$0–$791,275] and $12,912 [$0–$171,914]; 6–9 months: $43,914 [$112–$276,029] and $7,998 [$0–$52,802]; 9–12 months: $38,482 [$0–$256,287] and $7,462 [$0–$67,002]) in the commercially-insured and Medicaid-insured populations, respectively).

Figure 2. Annualized all-cause HRU among patients receiving a pediatric LT in the commercially-insured population (A) and the Medicaid-insured population (B).



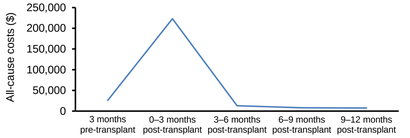
Box-and-whisker plots represent the median, interquartile range, and range of the overall annualized cost data; asterisks denote mean values. Max. value denotes the upper limit of the range, which is off-scale.

Figure 3. All-cause total medical costs by 3-month period in commercially-insured patients who had ≥12 months of continuous eligibility post-LT date.



Ranges for costs were: 3 months pre-transplant $0–$283,191; 0–3 months post-transplant $1,208–$2,052,575; 3–6 months post-transplant $0–$791,275; 6–9 months post-transplant $112–$276,029; 9–12 months post-transplant $0–$256,287.

Figure 4. All-cause total medical costs by 3-month period in Medicaid-insured patients who had ≥12 months of continuous eligibility post-LT date.

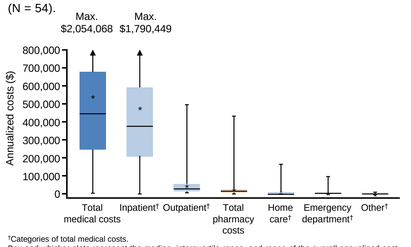


Ranges for costs were: 3 months pre-transplant $0–$467,971; 0–3 months post-transplant $0–$768,590; 3–6 months post-transplant $0–$171,914; 6–9 months post-transplant $0–$52,802; 9–12 months post-transplant $0–$67,002.

All-cause costs

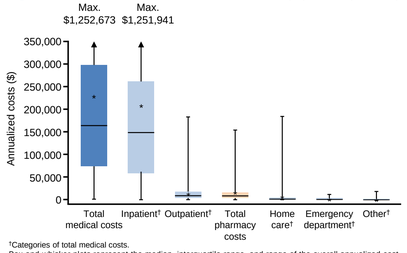
- Annualized mean medical costs among commercially-insured patients were $540,678 (range $1,066–$2,054,068 per year) (**Figure 5**).
  - The majority of these costs were incurred during inpatient visits (mean $477,516; range $0–$1,790,449).
- Annualized mean medical costs incurred by Medicaid-insured patients were $229,363 (range $176–$1,252,673 per year) (**Figure 6**).
  - As with the commercially-insured population, the majority of costs incurred by the Medicaid-insured population were due to inpatient visits (mean $209,256; range $0–$1,251,941 per year).

Figure 5. Annualized costs in the commercially-insured population (N = 54).



†Categories of total medical costs.
Box-and-whisker plots represent the median, interquartile range, and range of the overall annualized cost data; asterisks denote mean values. Max. value denotes the upper limit of the range, which is off-scale.

Figure 6. Annualized costs in the Medicaid-insured population (N = 108).



†Categories of total medical costs.
Box-and-whisker plots represent the median, interquartile range, and range of the overall annualized cost data; asterisks denote mean values. Max. value denotes the upper limit of the range, which is off-scale.

Limitations

- This analysis relied on diagnostic and treatment codes, which, being designed for administrative purposes, may have led to the misclassification of patients, and the underrepresentation of diagnoses and procedures. Furthermore, the analysis was unable to determine the burden of specific cholestatic liver diseases, such as Alagille syndrome and progressive familial intrahepatic cholestasis, due to the lack of specific International Classification of Diseases codes.
- The HRU and cost burden presented in the analysis do not necessarily reflect all costs incurred, but only costs reimbursed by insurers. Several factors, such as out-of-pocket expenses, e.g. transportation costs, the lifelong need for immunosuppression or re-transplantation, loss of education and wages, and the societal impact of these diseases were unaccounted for. Moreover, the costs of pharmacologic treatments were likely underreported in this database.
- The economic burden reported in this analysis is an estimation based on the costs reported during the study period and does not reflect the immunosuppression and monitoring with late graft complications required for children.
- The small sample sizes limit the power of these conclusions.

Conclusions

- **This analysis demonstrates that pediatric LTs, which are performed primarily due to cholestatic liver disease,[2] resulted in substantial HRU and cost burden in both the commercially-insured and Medicaid-insured populations, which was primarily driven by lengthy inpatient stays.**
- **The number of healthcare visits and associated costs ranged widely across patients, with some patient outliers experiencing a very high number of appointments and incurring very high costs.**
- **The largest economic burden was experienced in the first 0–6 months post-transplant; however, on average, patients continued to require significant healthcare visits and incur costs in the 6 months that followed this initial period.**
- **Optimization of medical management to slow the progression of liver disease and fibrosis in cholestatic liver disorders is needed. Novel targeted medications may delay or negate the need for LT and could decrease the morbidity and cost associated with LT.**

Contact information

Tamir Miloh, txm760@med.miami.edu

This poster was presented at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting® Digital Experience (TLMdX); November 12–15, 2021.

References

1. Bucuvalas JC, Zeng L, Anand R. The Studies of Pediatric Liver Transplantation (SPLIT) Research Group. Predictors of length of stay for pediatric liver transplant recipients. *Liver Transpl* 2004;10:1011–1017.
2. Kwong A, Kim WR, Lake JR, *et al*. OPTN/SRTR 2018 Annual Data Report: Liver. *Am J Transplant* 2020;20 Suppl s1:193–299.
3. Muiesan P, Vergani D, Mieli-Vergani G. Liver transplantation in children. *J Hepatol* 2007;46:340–348.
4. Kelly DA, Bucuvalas JC, Alonso EM, *et al*. Long-term medical management of the pediatric patient after liver transplantation: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver Transpl* 2013;19:798–825.
5. Soltys KA, Mazariegos GV, Squires RH, *et al*. Late graft loss or death in pediatric liver transplantation: an analysis of the SPLIT database. *Am J Transplant* 2007;7:2165–2171.
6. Wallot MA, Mathot M, Janssen M, *et al*. Long-term survival and late graft loss in pediatric liver transplant recipients--a 15-year single-center experience. *Liver Transpl* 2002;8:615–622.
7. Abramson O & Rosenthal P. Current status of pediatric liver transplantation. *Clin Liver Dis* 2000;4:533–552.
8. Kim WR, Brown RS Jr, Terrault NA, *et al*. Burden of liver disease in the United States: summary of a workshop. *Hepatology* 2002;36:227–242.
9. Tannuri ACA, Lima F, de Mello ES, *et al*. Prognostic factors for the evolution and reversibility of chronic rejection in pediatric liver transplantation. *Clinics (Sao Paulo)* 2016;71:216–220.
10. Spada M, Riva S, Maggiore G, *et al*. Pediatric liver transplantation. *World J Gastroenterol* 2009;15:648–674.
11. Cañon Reyes I, Esteban H, Diego A, *et al*. Prognostic factors in pediatric early liver retransplantation. *Liver Transpl* 2020;26:528–536.
12. Deshpande RR, Rela M, Girlanda R, *et al*. Long-term outcome of liver retransplantation in children. *Transplantation* 2002; 74:1124–1130.
13. Organ Procurement and Transplantation Network. Transplants in the U.S. by Recipient Age. Accessed online at: https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/# on August 2, 2021.
14. Lykavieris P, Chardot C, Sokhn M, *et al*. Outcome in adulthood of biliary atresia: a study of 63 patients who survived for over 20 years with their native liver. *Hepatology* 2005;41:366–371.
15. Kamath BM, Stein P, Houwen RHJ, *et al*. Potential of ileal bile acid transporter inhibition as a therapeutic target in Alagille syndrome and progressive familial intrahepatic cholestasis. *Liver Int* 2020;40:1812–1822.
16. Vandriel S, Li L, She H, *et al*. Clinical features and natural history of 1154 Alagille syndrome patients: results from the international multicenter GALA study group. *J Hepatol* 2020;73:S554–S555 (including poster presentation).
17. van Wessel DBE, Thompson RJ, Gonzales E, *et al*. Genotype correlates with the natural history of severe bile salt export pump deficiency. *J Hepatol* 2020;73:84–93.

Acknowledgments

This analysis was funded by Mirum Pharmaceuticals, Inc.
The authors thank Noam Kirson and Annika Anderson of Analysis Group, Inc. for their helpful comments and statistical guidance.
Medical-writing support for the development of this poster was provided by Charlotte Rowan, PhD, of Health Interactions, and funded by Mirum Pharmaceuticals, Inc.

Disclosures

T Miloh is a consultant for Mirum Pharmaceuticals, Inc.
A Goldstein and R Howard are full-time employees of and shareholders in Mirum Pharmaceuticals, Inc.
J R Marden and K Gaburo are full-time employees of Analysis Group, Inc., which received support from Mirum Pharmaceuticals, Inc. for participation in this research.
P Rosenthal has received grant support from Gilead Sciences, Inc., AbbVie, Travere Therapeutics, Mirum Pharmaceuticals, Inc., Albireo Pharma, Inc., and Arrowhead Pharmaceuticals, Inc., and is a consultant for Gilead Sciences, Inc., AbbVie, Travere Therapeutics, Mirum Pharmaceuticals, Inc., Albireo Pharma, Inc., Audentes Therapeutics, BioMarin Pharmaceutical, Inc., Dicerna Pharmaceuticals, Inc., Encoded Therapeutics, Inc., MedinCell, and Vertex Pharmaceuticals, Inc.