Claims Database Analysis of Health Care Resource Utilization and Associated Medical Costs in Patients with Barth Syndrome in the United States

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BACKGROUND

- Barth syndrome (BTHS) is a serious, X-linked ultra-rare genetic disorder with an estimated prevalence of ~1 in 1,000,000 male births[1]
- The US FDA has accepted a New Drug Application (NDA) for elamipretide HCl, the first disease-specific treatment for BTHS, supported by positive data from a Phase-3 Natural History Control Study[2] and additional supporting efficacy and safety data from TAZPOWER Open Label Extension (OLE)[3]
- Real-world patient data from the Stealth BioTherapeutics' Expanded Access Program (EAP) also illustrate the transformative potential of elamipretide in addressing severe, refractory cardiac dysfunction in BTHS, demonstrating the therapeutic value of the treatment[4-6]
- Clinical trials for orphan drugs conducted with small patient populations and real-world patient data can establish efficacy and safety, but economic evaluations of orphan drugs aimed at treating rare orphan diseases are more challenging[7]
- Policymaker reimbursement decisions after drug approval are largely based on efficacy and safety data, along with evidence-based implications from health economic evaluations; however, commonly used cost-effectiveness assessments are not applicable to orphan drugs[7,8]
- The small sample sizes of patients, along with the high development costs of orphan drugs, lead to polarized benefit assessment results[8]
- Rare diseases are often associated with increased severity and mortality, which further complicates the assessment of benefit indicators[8]
- One direct method to measure disease burden of rare diseases is overall cost and health care resource utilization (HCRU)[9]

OBJECTIVE

- A claims database analysis was conducted to assess HCRU and associated costs in the United States for patients with BTHS

METHODS

- Claims containing the ICD-10-CM diagnostic code for BTHS (E78.71) were examined using Healthcare Cost and Utilization Project (HCUP) data from the National (Nationwide) Inpatient Sample (NIS)[10] (combined 2020-2021 data) and the Kids' Inpatient Database (KID)[11] (2019 data) (**Table 1**)
- Claims were reviewed to ensure that results did not include ophthalmology visits, and one visit attributed to the BTHS ICD-10 code for ophthalmology-related appointment considered to be "unlikely BTHS" was removed
- Unweighted data were used for the current analysis since BTHS is an ultra-rare disease

Table 1. Overview of the Healthcare Cost and Utilization Project Databases: NIS and KID

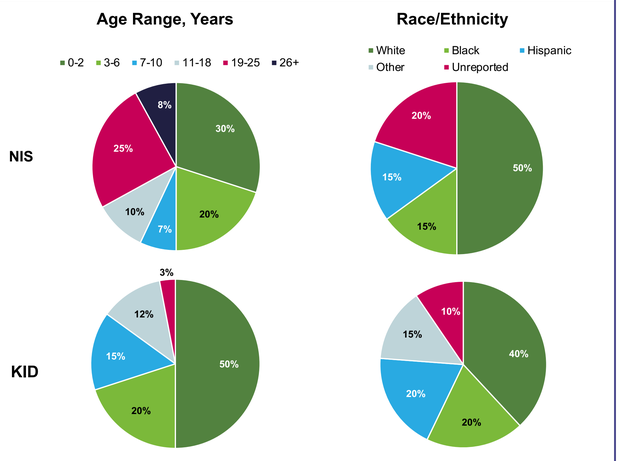
National (Nationwide) Inpatient Sample (NIS)[10]	• Largest publicly available all-payer inpatient healthcare database • Provides US regional and national estimates of inpatient utilization, access, cost, quality, payer, and outcomes • Unweighted, it contains data from ~7 million hospital stays each year
Kids' Inpatient Database (KID)[11]	• Largest US publicly-available all-payer pediatric inpatient care database • Contains clinical and resource-use information, including primary/secondary diagnoses and procedures, discharge status, patient demographics (e.g., sex, age, race), hospital characteristics (e.g., ownership, size, teaching status), expected payment source, total charges, length of stay, and severity measures • Unweighted, it contains data from ~3 million pediatric hospital discharges each year

- Complications or comorbidities (CC), major complications or comorbidities (MCC), procedure codes, patient age, length of stay, total charge, and total cost per claim were assessed from the NIS and KID datasets
- Case Mix Index (CMI) was assessed to measure the complexity and severity of patient cases
  - Typical CMI range is between 0.5 and 2.0
  - Higher CMI indicates more complex patient populations requiring greater HCRU
- Cost-to-Charge Ratio for Inpatient Files (CCR), defined as the ratio of hospital charges to costs, was used to estimate resource costs of inpatient care
- Descriptive (e.g., averages, medians) data were compared to better understand outliers

RESULTS

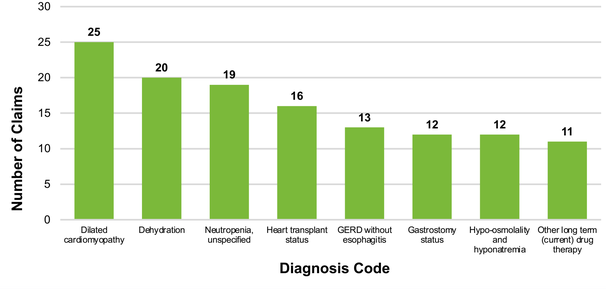
- There were 65 claims identified for BTHS in the KID and NIS databases (multiple claims for individual patients)
- As would be expected with BTHS, both datasets were 100% male claims, with age and race being similar in the NIS and KID database claims (**Figure 1**)
- Average (median) age was 11.2 (6) years for patients in the NIS and 4.7 (3) years for patients in the KID

Figure 1. Age and Race Data for Patient Claims from the NIS and KID



- Greater than 400 diagnostic codes (ICD-10-CM) were reported, demonstrating a significant number of comorbidities
- Common claims in the databases included dilated cardiomyopathy (n=25), dehydration (n=20), neutropenia (n=19), and heart transplant status (n=16) (**Figure 2**)

Figure 2. Diagnosis Codes Common to Both NIS and KID Datasets



GERD, gastro-esophageal reflux disease.

- NIS data included 47 different Medicare Severity Diagnosis-Related Groups (MS-DRGs) (**Table 2**)
  - Of those, 24 were MCCs (including ventilator MS-DRGs) and 10 were CCs

Table 2. Medicare Severity Diagnosis-Related Groups in the NIS Dataset with and Without MCCs and CCs

MS-DRGs with MCCs
Aftercare with CC/MCC
Bronchitis and asthma with CC/MCC
Cardiac arrhythmia and conduction disorders with MCC
Cellulitis with MCC
Diabetes with MCC
Disorders of pancreas except malignancy with MCC (2)*
Esophagitis, gastroenteritis and miscellaneous digestive disorders with MCC
Gastrointestinal hemorrhage with MCC
Major hematological and immunological diagnoses except sickle cell crisis and coagulation disorders with MCC
Miscellaneous disorders of nutrition, metabolism, fluids and electrolytes with MCC (2)*
Otitis Media and upper respiratory infection with MCC
Other circulatory system diagnoses with MCC (3)*
Other musculoskeletal system and connective tissue diagnoses with MCC
Other respiratory system operating room (OR) procedures with MCC
Percutaneous and other intracardiac procedures with MCC
Respiratory infections and inflammations with MCC (2)*
Stomach, esophageal and duodenal procedures with MCC
Seizures with MCC
Simple pneumonia and pleurisy with MCC
MS-DRGs with CCs
Appendectomy without complicated principal diagnosis with CC
Heart failure and shock with CC
Laparoscopic cholecystectomy without common duct exploration (C.D.E.) with CC
Major gastrointestinal disorders and peritoneal infections with CC
Major hematological and immunological diagnoses except sickle cell crisis and coagulation disorders with CC (2)
Other circulatory system diagnoses with CC
Other musculoskeletal system and connective tissue diagnoses with CC
Respiratory infections and inflammations with CC
Simple pneumonia and pleurisy with CC
MS-DRGs Without MCC/CC
Circulatory disorders except acute myocardial infarction (AMI), with cardiac catheterization
Extreme immaturity or respiratory distress syndrome, neonate (2)*
Miscellaneous disorders of nutrition, metabolism, fluids and electrolytes (2)*
Neonate with other significant problems
Otitis media and upper respiratory infection (2)*
Poisoning and toxic effects of drugs
Respiratory system diagnosis with ventilator support >96 hours (2)*
Septicemia or severe sepsis without mechanical ventilation >96 hours (2)*

CC, Complications or comorbidities; MCC, major complications or comorbidities; MS-DRG, Medicare Severity Diagnosis-Related Groups.

*Numbers in parentheses are median values.

- Average length of stay (ALOS) was 8.2 days (median at 3.0 days) in the NIS and 14.8 days (median at 6.0 days) in the KID (**Table 3**)
- Average hospital wage index was similar between KID (1.02) and NIS (1.06) and comparable to the national average (1.0)
- Average hospital CCR for KID (0.247) was lower than NIS (0.303)
- Charge amounts showed similar results for both datasets
  - Average total charge per claim in NIS was $127,324 (median value $52,345)
  - In KID, average total charge per claim was $218,789 (median value $45,927)
- Hospital cost per claim showed similar results for both datasets
  - The NIS average hospital cost per claim was $32,702 (median, $17,326)
  - The KID average hospital total cost per claim was $62,596 (median, $13,647)
- CMI (a severity metric with higher values indicating more severity) averaged 2.01 (median value 1.37) in NIS and 1.59 (median value 1.03) in KID
- An average of 49% to 51% of cases in the NIS were Medicaid/Private Pay

Table 3. NIS and KID Data for Assessed Variables

Variable	NIS		KID	
	Average	Median	Average	Median
Length of Stay (Days)	8.2	3	14.8	6
Average Total Charge	$127,324[a]	$52,345	$218,789[a]	$45,927
CMI	2.01[a]	1.37	1.59[a]	1.03
Average Total Cost	$32,702[a]	$17,326	$62,596[a]	$13,647
Average Hospital Wage Index[b]	1.06	0.961	1.02	0.966
Average Hospital CCR	0.303	0.269	0.274	0.253

CMI, Case Mix Index; CCR, Cost-to-Charge Ratio.

[a]Outliers and ventilator support >96 hours skew averages high. [b]National Average is 1.

CONCLUSIONS

- Data extrapolated during this claims database analysis demonstrated that patients with diagnostic codes linked to BTHS are complex patients with a high percentage of complications
- This high degree of complexity in patients with BTHS can become significant, necessitating a high level of HCRU and associated costs in the inpatient setting

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