Claims Database Analysis to Assess the Complexity and Severity of Patient Cases, Disease Burden, and Health Care Resource Utilization (HCRU) in US Barth Syndrome Patients

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BACKGROUND

- Barth syndrome (BTHS) is a serious, ultra-rare genetic disorder with an estimated prevalence of ~1 in 1,000,000 male births[1]
- US FDA granted accelerated approval to elamipretide as the first treatment for BTHS[2]
  - Approval was supported by positive data from a Phase-3 natural history control study2 and efficacy and safety data from TAZPOWER open label extension[3] showing improvement in functional assessments and cardiac function along with sustained tolerability
- Commonly used cost-effectiveness assessments are not applicable to orphan drugs, making economic evaluation of approved treatments for orphan diseases challenging[4,5]
- Clinical trials for orphan drugs are conducted with small patient populations, and rare diseases are often associated with increased severity and mortality,[6] which further complicates the assessment of benefit indicators[5,7]
- One direct method to measure disease burden of rare diseases is overall cost and health care resource utilization (HCRU)[8]
- To support reimbursement of the first disease-specific treatment for BTHS, the economic evaluation of elamipretide is necessary

OBJECTIVE

- A claims database analysis was conducted to describe the complexity and severity of patient cases, to measure disease burden, and to assess HCRU for patients with BTHS in the US

METHODS

- Claims containing the ICD-10 diagnostic code for BTHS (E78.71) were identified using Healthcare Cost and Utilization Project (HCUP) data from the National (Nationwide) Inpatient Sample (NIS)[9] (combined 2020, 2021, 2022, and 2023 data for all ages) and the Kids' Inpatient Database (KID)[10] (2019 and 2022 data for patients <21 years of age) (**Table 1**)

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

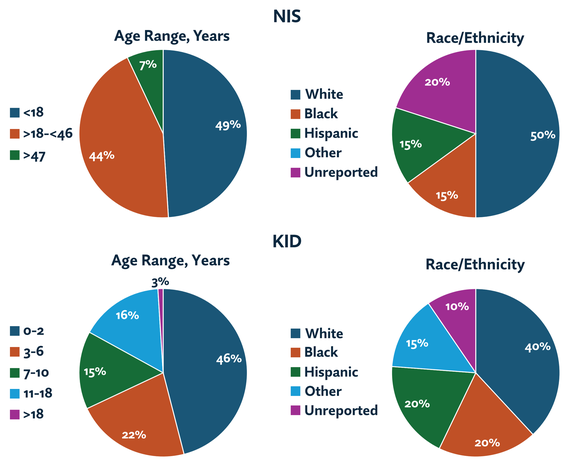
National (Nationwide) Inpatient Sample (NIS)[9]	• Largest publicly available all-payer inpatient healthcare database • Provides US regional and national estimates of inpatient utilization, access, cost, quality, payer, and outcomes • Unweighted, it contains data from ~7 million hospital stays each year
Kids' Inpatient Database (KID)[10]	• 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

- Claims were reviewed to ensure that results did not include ophthalmology visits and for male vs. female subjects
  - One visit attributed to the BTHS ICD-10 code for ophthalmology-related appointment considered to be "unlikely BTHS" was removed
- Inventory of primary and secondary diagnosis codes where BTHS (E78.71) was present was assessed to measure the complexity and severity of patient cases
- Unweighted data were used for the current analysis since BTHS is an ultra-rare disease, but some select analyses were estimated on a national basis
- Claims from the KID and NIS databases were separated (not aggregated) for analysis
- Claim counts stratified by age range (groups: 0-4, 5-12, and 13-20 years, inclusive) were assessed from the KID data
- NIS age ranges were stratified by groups under 19, 19-45 and >45 years
- Medicare Severity Diagnosis-Related Groups (MS-DRGs) were analyzed for highest volume MS-DRGs for BTHS in NIS and KID data
- Complications or comorbidities (CC), major complications or comorbidities (MCC), procedure codes, patient age, average length of stay (ALOS), and average total charge were examined for NIS and KID data

RESULTS

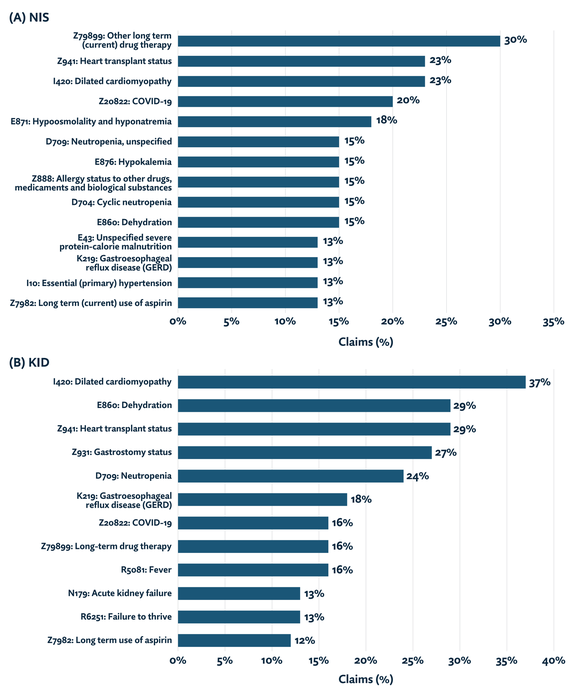
- Seventy claims for BTHS were identified in the NIS databases, and 68 claims were identified for BTHS in KID databases (multiple claims for individual patients)
- Both datasets were 100% male claims
- Age and race for NIS and KID database claims are found in **Figure 1**
- Average (median) age was 20.65 (20) years for subjects in the NIS and 4.98 (3) years for subjects in the KID

Figure 1. Age and Race Data for Patient Claims From NIS and KID Databases



- >300 diagnostic codes (ICD-10-CM) were reported with BTHS claims, demonstrating a significant number of comorbidities
- Common claims with BTHS included dilated cardiomyopathy (23% NIS; 37% KID), dehydration (15% NIS; 30% KID), neutropenia (15% NIS; 24% KID), heart transplant status (23% NIS; 30% KID), and other long term (current) drug therapy (30% NIS; 16% KID) (**Figure 2**)

Figure 2. Common (>11%) Primary and Secondary ICD-10 Diagnosis Codes Present With BTHS (E78.71): NIS and KID



- Common claims (>11%) in the KID by age range revealed that dehydration and neutropenia were seen in each of the three age groups assessed (**Table 2**)
- Dilated cardiomyopathy was the twelfth most common primary diagnosis code for the 0-4 age group but was not a common primary code in the other age groups

Table 2. Primary Diagnosis Codes (>11%) by Age Group in Descending Order From KID

ICD-10 Diagnosis Code	Description
Aged 0-4 years (inclusive)	
Z3800	Single liveborn infant, delivered vaginally
E7871	BTHS
E860	Dehydration
D704	Cyclic neutropenia
E440	Moderate protein-calorie malnutrition
J159	Unspecified bacterial pneumonia
A0472	Enterocolitis due to *Clostridium difficile*, not specified
A0811	Acute gastroenteropathy due to Norwalk agent
D700	Congenital agranulocytosis
G40901	Epilepsy, unspecified, not intractable, with status epilepticus
H6693	Otitis media, unspecified, bilateral
I420	Dilated cardiomyopathy
I424	Endocardial fibroelastosis
I5021	Acute systolic (congestive) heart failure
A020	Salmonella enteritis
J069	Acute upper respiratory infection, unspecified
Z3831	Twin liveborn infant, delivered by cesarean
J189	Pneumonia, unspecified organism
J210	Acute bronchiolitis due to respiratory syncytial virus (RSV)
J690	Pneumonitis due to inhalation of food and vomit
J9601	Acute respiratory failure with hypoxia
K529	Noninfective gastroenteritis and colitis, unspecified
P0703	Extremely low birth weight newborn, 750-999 grams
P290	Neonatal cardiac failure
Q549	Hypospadias, unspecified
R6251	Failure to thrive (child)
T39011A	Poisoning by aspirin, accidental (unintentional)
T8621	Heart transplant rejection
T86298	Other complications of heart transplant
I5043	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
Aged 5-12 years (inclusive)	
J101	Influenza due to other identified influenza virus
D709	Neutropenia, unspecified
A419	Sepsis, unspecified organism
T82524A	Displacement of infusion catheter, initial encounter
R1110	Vomiting, unspecified
N179	Acute kidney failure, unspecified
K3580	Unspecified acute appendicitis
K220	Achalasia of cardia (difficulty swallowing)
J4521	Mild intermittent asthma with (acute) exacerbation
J1289	Other viral pneumonia
I674	Hypertensive encephalopathy
E860	Dehydration
D700	Congenital agranulocytosis
Aged 13-20 years (inclusive)	
M7989	Other specified soft tissue disorders
J069	Acute upper respiratory infection, unspecified
E860	Dehydration
E7871	BTHS
E09649	Drug or chemical induced diabetes mellitus with hy
D709	Neutropenia, unspecified
D708	Other neutropenia
D700	Congenital agranulocytosis

- KID and NIS data included 47 different MS-DRGs
  - Of those, 24 were MCCs (including ventilator MS-DRGs) and 10 were CCs
- MS-DRG 809 (major hematological and immunological diagnoses) was the highest volume MS-DRG for BTHS in NIS and KID (**Table 3**)

Table 3. Highest Volume MS-DRGs for BTHS: NIS and KID

MSDRG	Description
NIS	
809	Major hematological and immunological diagnoses except sickle cell crisis and coagulation disorders with CC
291	Heart failure and shock with MCC
640	Miscellaneous disorders of nutrition, metabolism, fluids and electrolytes with MCC
872	Septicemia or severe sepsis without mv >96 hours without MCC
314	Other circulatory system diagnoses with MCC
391	Esophagitis, gastroenteritis and miscellaneous digestive disorders with MCC
KID	
809	Major hematological and immunological diagnoses except sickle cell crisis and coagulation disorders with CC
641	Miscellaneous disorders of nutrition, metabolism, fluids and electrolytes without MCC
194	Simple pneumonia and pleurisy with CC
001	Heart transplant or implant of heart assist system with MCC
565	Other musculoskeletal system and connective tissue diagnoses with CC
391	Esophagitis, gastroenteritis and miscellaneous digestive disorders with MCC
003	ECMO or tracheostomy with MV >96 hours or principal diagnosis except face, mouth and neck with major O.R. procedures

- For the highest volume MS-DRG in NIS and KID data (809: major hematological and immunological diagnoses except sickle cell crisis and coagulation disorders with CC):
  - ALOS ranged from 1 to 7 days (mean 3.4 days)
  - Average total charge per claim ranged from $6,443 to $65,619 (median value $29,789)
  - Average cost per claim ranged from $2,584 to $18,373 (median value $7,924)
- Dilated cardiomyopathy and dehydration were common for the highest volume code (809)
  - Dilated cardiomyopathy ALOS was 2.0 days; average charge was $15,838; average cost was $4,871
  - Dehydration ALOS was 2.0 days; average charge was $19,266; average cost was $5,364
- ALOS was 12.9 days (median at 3.0 days) in the NIS and 14.7 days (median at 3.0 days) in the KID (**Table 4**)
- Charge amounts showed similar results for NIS and KID
  - Average total charge per claim in NIS was $302,072 (median value $38,861)
  - In KID, average total charge per claim was $254,625 (median value $37,427)

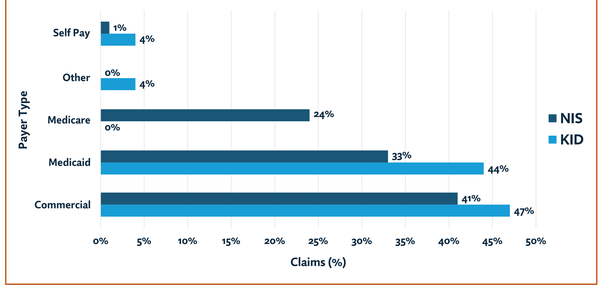
Table 4. KID and NIS Data for Assessed Variables

Variable	NIS		KID	
	Average	Median	Average	Median
Length of Stay (Days)	12.9	3	14.7	3
Average Total Charge	$302,072[a]	$38,861	$254,625[a]	$37,427

[a]Outliers and ventilator support >96 hours skew averages high.

- Although only 7% of subjects were older than 45 years in NIS, payer type for 24% of claims was Medicare (**Figure 3**)

Figure 3. Payer Type for Claims: NIS and KID Databases



- Mortality was 4.4% in KID and 2.85% in NIS; deaths reported in KID were all newborns, with many on Extracorporeal Membrane Oxygenation (ECMO)

CONCLUSIONS

- Data extrapolated during this claims analysis demonstrated that patients with diagnostic codes linked to BTHS are highly complex with frequent comorbidities
- 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
- Elamipretide recently received FDA accelerated approval for BTHS, which may help to alleviate disease-related HCRU for these complex patients

References:

1. Miller PC, et al. *J Pediatr*. 2020;217:139–144. **2.** US FDA. FDA grants accelerated approval to first treatment for Barth syndrome. Accessed April 14, 2026. Available at: https://content.govdelivery.com/accounts/USFDA/bulletins/3f38219. **3.** Hornby B, et al. *Orphanet J Rare Dis*. 2022;17(1):336. **4.** Thompson WR, et al. *Genet Med*. 2024:101138. **5.** Grand TS, et al. *Pharmacoeconomics*. 2024;42(6):619–631. **6.** Fu K, et al. *J Inherit Metab Dis*. 2026;49(3):e70189. **7.** Zhang X, et al. *BMC Health Serv Res*. 2024;24(1):1123. **8.** Navarrete-Opazo AA, et al. *Genet Med*. 2021;23(11):2194–2201. **9.** HCUP Databases. Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality, Rockville, MD. Overview of the National (Nationwide) Inpatient Sample (NIS). Accessed April 14, 2026. Available at: https://hcup-us.ahrq.gov/nisoverview.jsp. **10.** HCUP Databases. Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality, Rockville, MD. Overview of the Kids' Inpatient Database (KID). Accessed April 14, 2026. Available at: https://hcup-us.ahrq.gov/kidoverview.jsp.

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