Treatment Patterns and Costs of Care in Commercially-Insured and Medicaid Patients with Transfusion-Dependent β-Thalassemia

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BACKGROUND

- β-thalassemia is a genetic disease, characterized by reduced or absent synthesis of beta-globin, ineffective erythropoiesis and hemolysis, that can lead to anemia and other complications.[1]
- Depending on severity and clinical management it is grouped into transfusion-dependent (TDT) and non-transfusion dependent β-thalassemia (NTDT).
- Patients with TDT require frequent and life-long red blood cell (RBC) transfusions for survival. Chronic transfusions introduce excess iron, requiring rigorous monitoring of iron burden and life-long iron chelation therapy.
- Despite improvements in iron chelation treatment and monitoring, TDT is associated with increased morbidity and mortality.
- Allogeneic hematopoetic stem cell transplant (allo-HSCT) is a potential treatment option for some TDT patients with a matched donor.[2,3]
- There are limited data available on the costs of treating patients with TDT in the U.S.[4]

OBJECTIVES

- To examine costs of care for TDT patients including standard of care with RBC transfusions and iron chelation therapy, as well as costs for an episode of care with allo-HSCT.
- To examine predictors of costs of TDT patient care.

METHODS

Data Source

- This study utilized patient-level, de-identified U.S. administrative claims data from the Truven Health MarketScan® Commercial, Medicare Supplemental, and Medicaid Multi-State Databases, for the period from January 1, 2006 to June 30, 2017 (specific inclusion dates described below).
- These databases include medical encounter and outpatient pharmacy data covering roughly 43 million enrollees per year linked by a unique blinded identifier across the continuum of care.
- The MarketScan Research Databases are de-identified, fully compliant with the Health Insurance Portability and Accountability Act of 1996 and are representative of the US managed-care population.

TDT Patient Identification

- Patients meeting the following criteria were included in the TDT cohort
  - ≥8 RBC transfusions in a given 12-month period (first transfusion date = TDT index date) between October 1, 2011 and September 30, 2016
  - ≥1 non-diagnostic claim with a β-thalassemia or hemoglobin E β-thalassemia diagnosis between 3 months before and 15 months after the TDT index date
  - No evidence of allo-HSCT between the first and eighth qualifying transfusions
  - ≥30 days of continuous enrollment after the TDT index date.
    - After this 30-day period, continuous enrollment was not required during the follow-up period for the TDT cohort

Allo-HSCT Patient Identification

- Patients meeting the following criteria were included in the Allo-HSCT cohort
  - ≥1 non-diagnostic claim with a diagnosis code for β-thalassemia or hemoglobin E β-thalassemia between January 1, 2010 and Septembber 30, 2016 for Commercial patients and between January 1, 2006 and June 30, 2016 for Medicaid patients.
  - ≥1 medical claim with a procedure code for allogeneic bone marrow or stem cell transplant between January 1, 2010 and September 30, 2016 for Commercial patients and between January 1, 2006 and June 30, 2016 for Medicaid patients.
  - The AT index date was defined as the date of the transplant.
  - ≥12 months of continuous enrollment after the AT index date.

Follow-up Periods

- For the TDT cohort, the follow-up period was variable in duration and extended from the TDT index date until the date of the earliest of the following: (1) allogeneic bone marrow or stem cell transplant; (2) end of database enrollment; or (3) end of the study period.
- For the Allo-HSCT cohort, the follow-up period was the fixed, 12-month period after the AT index date.

Study Variables and Outcomes

- Demographic characteristics: age, gender, plan type, payer, geographic region
- Comorbid conditions: cirrhosis, diabetes, heart failure, hemochomatosis, hypogonadism, kidney disease, osteoporosis
- β-thalassemia-related events: RBC transfusions, iron chelation therapy, iron overload monitoring, iron complications (hemochromatosis and splenectomy, excision/resection of the spleen)
- For the TDT cohort, demographic characteristics were measured on the TDT index date. The annual number of RBC transfusions and annual treatment costs were measured over the variable follow-up period. Per-patient-per year (PPPY) costs were calculated as follows:
  - PPPY = [Total costs during follow-up] ÷ [Total days covered during follow-up] * [365]
- Generalized linear modeling was used to identify predictors of high costs for the TDT cohort. Examined potential predictors included demographic characteristics, pre- or post-period comorbidities and pre- or post-period evidence of β-thalassemia-related events
- Annual costs for the allo-HSCT cohort included the transplant cost plus any additional costs for the first 12 months following the AT index date
- All dollar estimates were inflated to 2016 dollars using the Medical Care Component of the Consumer Price Index (CPI).

RESULTS

Sample Sizes and Baseline Characteristics

- There were 244 patients in the TDT cohort and 24 patients in the allo-HSCT cohort.
- Three quarters (75.0%) had commercial insurance, 23.4% were sampled from our <10 state Medicaid database, and 1.6% had Medicare coverage. Geographically, 32.8% lived in the Northeast, 25.8% in the Midwest, 25.8% in the South, and 15.6% in the West.

Table 1: Baseline Demographics of TDT Cohort

	N = 244	
	N/Mean	%/SD
Number of days between index date and end of follow-up period (Mean, SD)	831.5	497.9
Number of enrolled days between index date and end of follow-up period (Mean, SD)	815.3	490.7
Age (Mean, SD)	22.4	17.2
Female (N, %)	132	54.1%
Payer (N, %)		
Commercial	183	75.0%
Medicare	4	1.6%
Medicaid	57	23.4%
Geographic Region (N, %)		
Northeast	80	32.8%
Midwest	63	25.8%
South	63	25.8%
West	38	15.6%

RESULTS (continued)

Outcomes

- During the variable follow-up period (mean duration 831.5 days), TDT patients had a median of 15 transfusions annually (min-max: 8-138).
- 236/244 (81.1%) TDT patients had ≥1 prescription for iron chelation therapy (73.7% oral only, 7.1% injection only, 19.2% oral plus injection). 179/244 (73.4%) had an iron complication.
- 99.6% of TDT patients were being monitored for iron overload, and 75.5% had at least one iron overload complication.
- Mean transfusion-related costs in the TDT cohort were $29,292 PPPY (23.0% of total costs), chelation therapy costs were $51,974 PPPY (40.7% of total costs) and iron overload monitoring and complication costs were $10,674 PPPY (8.4% of total costs). Other PPY medical costs represented 27.9%.

Table 2: Characteristics and Costs of TDT Management During the Variable Follow-Up Period (N = 244)

	N/Mean	%/SD	Median	Min	Max
Number of transfusions, PPPY* (Mean, SD, Median)	15.9	6.8	15	8	138
Transfusion-related costs, PPPY (Mean, SD, Median)[1]	$29,292	$27,212	$22,433	$0	$189,185
Had Iron chelation therapy (N, %)	198	81.1%			
Iron chelation therapy-related costs, PPPY (Mean, SD, Median)	$51,974	$40,416	$43,309	$0	$165,245
Had iron overload monitoring[2]	236	99.6%			
Had iron overload complication[3]	179	73.4%			
Iron overload monitoring and complication costs, PPPY (Mean, SD, Median)					
Iron overload monitoring and complication costs	$10,674	$36,171	$2,330	$0	$496,101
Iron overload monitoring costs	$2,463	$12,962	$702	$0	$197,484
Iron overload complication costs	$10,666	$38,212	$2,377	$0	$494,728

* Minimums/ maximums reported across all follow-up and not annualized.
[1] Transfusion-related costs include costs on claims for transfusion procedures, outpatient office visits on the day of transfusion, and transfusion-related procedures (blood count, blood typing, injection, venipuncture, cutdown, and blood administration) in the 5 days before and after day of transfusion.
[2] Iron overload monitoring procedures included cardiac MRI and iron-related laboratory tests (iron, ferritin, transferrin, and iron binding capacity).
[3] Iron overload complications only included hemochromatosis and splenectomy, excision/resection of the spleen.

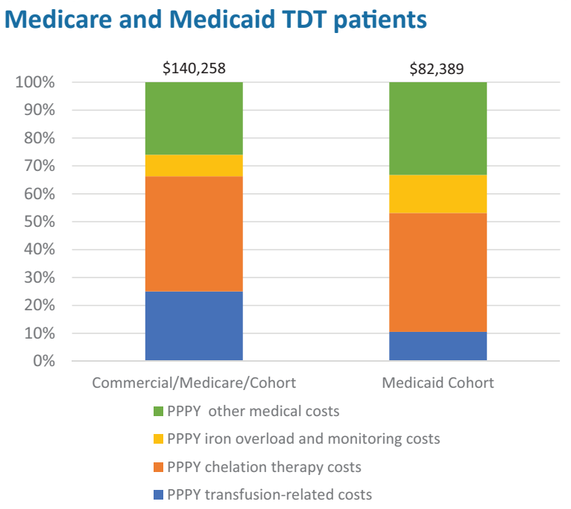
- Mean annual per-patient costs were $127,553 ± $122,511 (median $97,744; min-max $1,943-$1,223,683) for the TDT cohort
- Multivariate analysis found that Medicare or Medicaid coverage was a predictor of lower annual healthcare costs compared to commercial insurance, with p=0.023 and p=0.001, respectively. Post-index evidence of diabetes (p=0.040) and heart failure (p=0.037) were significantly associated with PPPY total healthcare cost, and the number of pre-index injectable iron chelation treatments was marginally predictive of healthcare costs (p=0.057).

Table 3: Predictors of high PPPY total healthcare cost in the TDT cohort

Predictor	Estimate	Lower 95% CL	Upper 95% CL	ChiSq	P-value
Payer: Medicare vs Commercial	0.288	0.099	0.842	5.17	0.023
Payer: Medicaid vs Commercial	0.554	0.387	0.793	10.43	0.001
Count of pre-index injectible iron chelation therapy	0.990	0.980	1.000	3.63	0.057
Evidence of diabetes post-index	1.530	1.019	2.298	4.21	0.040
Evidence of heart failure post-index	1.454	1.022	2.069	4.33	0.037

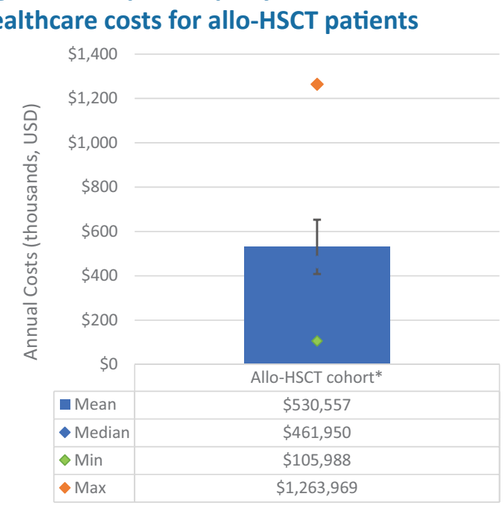
- Mean costs in the 12 months following allo-HSCT including transplant costs were $530,557 ± $340,416 (median $461,950; min-max $105,988-$1,263,969)

Figure 1: Distribution of per-person-per-year (PPPY) all-cause healthcare costs for Commercial/ Medicare and Medicaid TDT patients



*Annualized over the variable follow-up period

Figure 2: Per-person-per-year all-cause healthcare costs for allo-HSCT patients



*Annualized over the variable follow-up period; Costs for the 12-months following allo-HSCT procedure

LIMITATIONS

- This study was limited to only those individuals in the U.S. with commercial health insurance, Medicare coverage, or Medicaid coverage; therefore, the results may not be generalizable to patients with other insurance or without health insurance coverage.
- The misclassification of patients is possible due to coding error or gaps such as under-coding of inpatient blood transfusions because these claims do not affect reimbursement.
- To preserve the sample size, continous enrolment was not requried of patients in the TDT Cohort; therefore, it is possible that these patients acquired healthcare not captured in this analysis.

CONCLUSIONS

- Ongoing monitoring of iron overload, treatment for iron overload complications and management of comorbidities only represent a portion of total medical cost burden of TDT.
- Given the observed annual costs of treatment, the 10-year costs for chronic treatment of TDT can be in excess of $1M.

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