

Healthcare Resource Use, Economic Burden, and Inpatient Mortality in Patients With Alpha- or Beta-Thalassemia Compared With Matched Controls in the Real-World Setting

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BACKGROUND

- Alpha (α)- and beta (β)-thalassemia result from diminished synthesis of α- and β-globin, respectively.¹
- Both types of thalassemia lead to ineffective erythropoiesis, chronic hemolytic anemia (HA), and associated complications.²
- Limited research has been conducted in the US regarding healthcare resource utilization (HCRU) and economic burden across the full range of thalassemia subtypes, including α-thalassemia and non-transfusion-dependent β-thalassemia.³⁻⁵

OBJECTIVE

- To evaluate HCRU, costs, and inpatient mortality in patients with thalassemia compared with matched controls

METHODS

- Patients with thalassemia and matched controls were selected from:
 - Merative™ MarketScan® Commercial Database (private health insurance)^a
 - Merative™ MarketScan® Medicare Database (government health insurance for persons ≥65 years of age and/or disabled)^a
 - Merative™ MarketScan® Multi-State Medicaid Database (government health insurance for persons of low income)

Patients with thalassemia:

- Adults (≥18 years) with ≥2 claims in the outpatient or inpatient setting or ≥1 in the inpatient setting for α- or β-thalassemia International Classification of Diseases, Ninth Revision (ICD-9)/International Classification of Diseases, Tenth Revision (ICD-10) codes from January 1, 2013, to June 30, 2021
- ≥12 months of continuous enrollment (with medical and pharmacy benefits) after the index date
- No evidence of other HAs^b during follow-up

Controls:

- Individuals with no history of thalassemia or other HAs were matched 5:1 to patients with thalassemia on age, sex, payer, race/ethnicity (Medicaid only), and length of follow-up.
- Index date for thalassemia was defined as the first date of α- or β-thalassemia diagnosis code.
- Index dates for matched controls were randomly assigned, based on distribution of index dates of cases.

Condition	ICD-9-CM	ICD-10-CM
Alpha thalassemia (including Alpha thalassemia major, Hemoglobin H Constant Spring, Hemoglobin H disease, Hydrops fetalis due to alpha thalassemia, Severe alpha thalassemia, Triple gene defect alpha thalassemia)	282.43	D56.0
Beta thalassemia (including Beta thalassemia [Beta thalassemia major, Cooley's anemia, Homozygous beta thalassemia, Severe beta thalassemia, Thalassemia intermedia, Thalassemia major], Delta-beta thalassemia, and Hemoglobin E-beta thalassemia)	282.44 282.45 282.47	D56.1 D56.2 D56.5

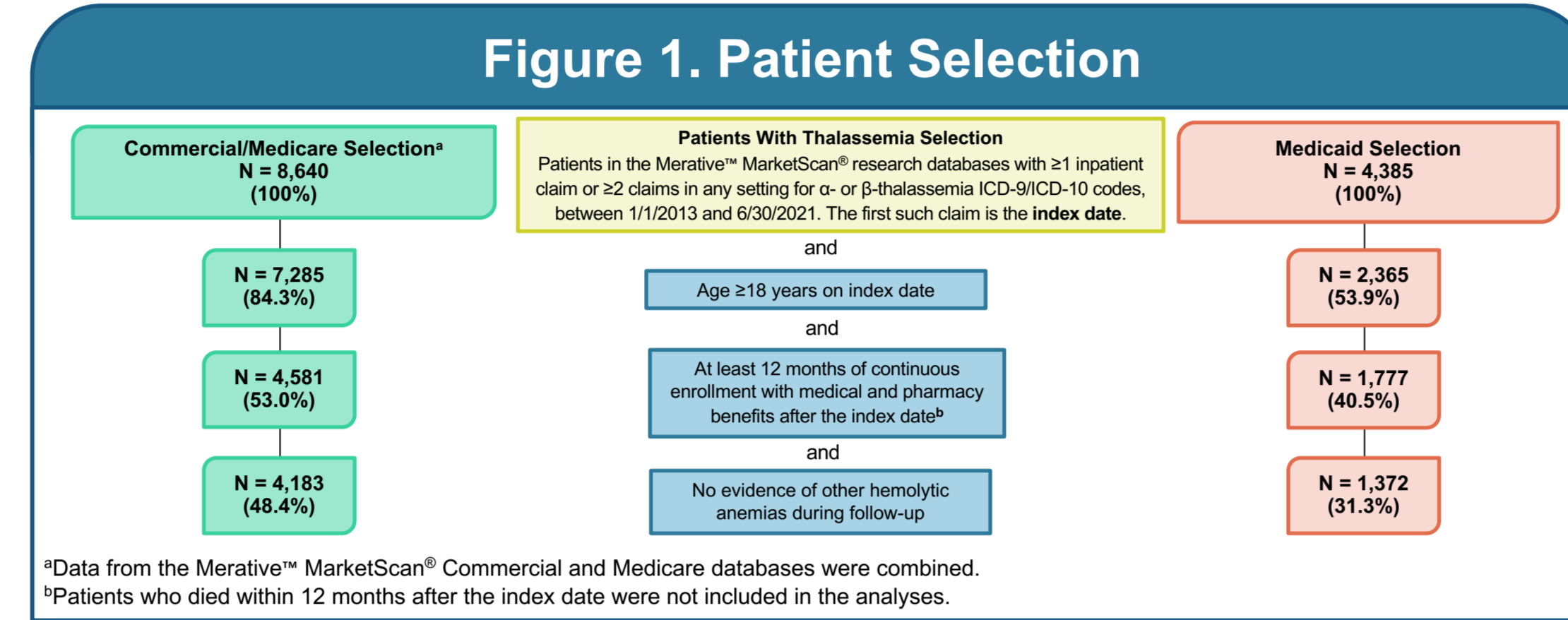
- HCRU and costs (in US dollars reported as per person per year [PPPY]) were assessed during the 12 months post index date.
 - All dollar estimates were inflated to 2020 dollars using the Medical Care Component of the Consumer Price Index (CPI).
- Inpatient mortality data were reported using a variable length follow-up period (minimum of 12 months from the index date to the end of enrollment, inpatient death, or study end (6/30/2021), whichever occurred first).
- Thalassemia cohorts were stratified by:
 - Thalassemia type (α- or β-thalassemia)
 - Transfusion dependence status
 - Non-transfusion-dependent thalassemia (NTDT)
 - Transfusion-dependent thalassemia (TDT)

TDT was defined as ≥8 transfusions within 12 months of follow-up, with <42 days between any 2 transfusions.

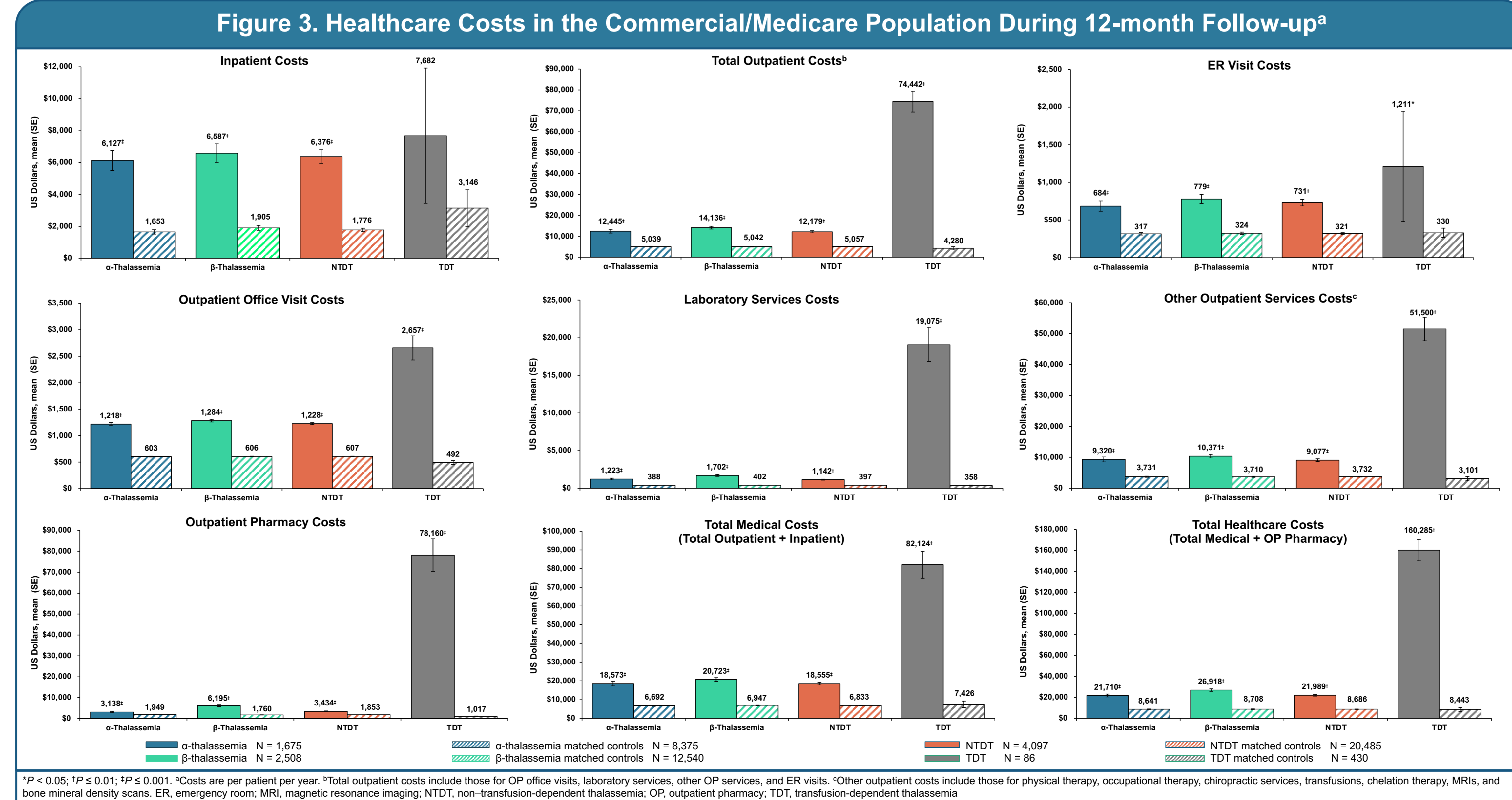
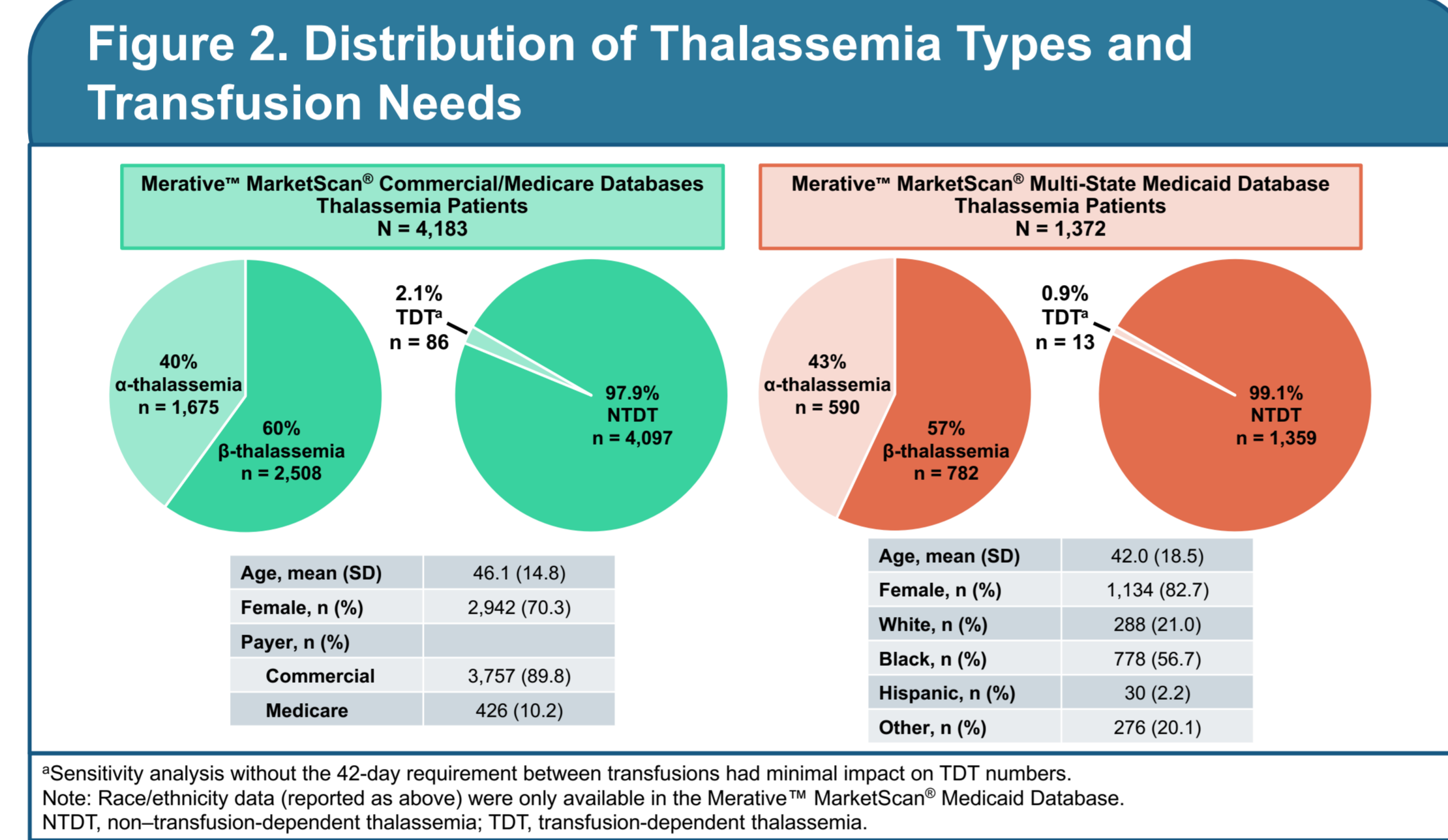
- Chi-square (categorical variables) and t-tests (continuous variables) were used for outcome comparisons, with 2-sided significance level of 0.05.

RESULTS

- Patients and controls were selected from the Merative™ MarketScan® research databases (Figure 1).



- Proportions of patients with α-thalassemia, β-thalassemia, TDT, and NTDT were similar among the Merative™ MarketScan® Commercial/Medicare and Medicaid databases (Figure 2).



- In the Commercial/Medicare population, most of the HCRU outcomes during the 12-month follow-up were significantly higher across all thalassemia cohorts compared with matched controls (Table 1).
- In the Medicaid population, most of the HCRU outcomes during the 12-month follow-up were also significantly higher across thalassemia cohorts compared with matched controls (Supplemental Table; see QR code).

Table 1. HCRU Burden in the Commercial/Medicare Population

	α-Thalassemia (N = 1,675)	α-Thalassemia Control (N = 8,375)	β-Thalassemia (N = 2,508)	β-Thalassemia Control (N = 12,540)	NTDT (N = 4,097)	NTDT Control (N = 20,485)	TDT (N = 86)	TDT Control (N = 430)
Patients with ≥1 inpatient admission, n (%)	331 (19.8)*	470 (5.6)	501 (20.0)*	737 (5.9)	819 (20.0)*	1,174 (5.7)	13 (15.1)*	33 (7.7)
Number of inpatient admissions, mean (SD) ^d	1.3 (0.6)	1.2 (0.6)	1.4 (1.0)*	1.2 (0.6)	1.3 (0.8)*	1.2 (0.6)	1.6 (1.0)	1.4 (1.3)
Patients with ≥1 outpatient service, n (%)	1,675 (100)*	7,497 (89.5)	2,507 (100)*	11,018 (87.9)	4,096 (100)*	18,161 (88.7)	86 (100)*	354 (82.3)
Patients with ≥1 ER visit, n (%)	487 (27.9)*	1,435 (17.1)	715 (28.5)	3,674 (29.3)	1,157 (28.2)*	3,803 (17.6)	25 (28.1)*	71 (16.5)
Patients with ≥1 outpatient office visit, n (%)	1,667 (99.9)*	7,176 (85.7)	2,494 (99.4)*	10,444 (83.3)	4,076 (99.5)*	17,298 (84.4)	85 (98.8)*	322 (74.9)
Number of outpatient office visits, mean (SD) ^d	9.2 (8.0)*	5.7 (5.5)	9.7 (8.7)*	5.9 (5.7)	9.4 (8.3)*	5.8 (5.6)	17.0 (13.1)*	5.2 (6.0)
Outpatient pharmacy								
Patients with ≥1 prescription, n (%)	1,520 (90.7)*	6,611 (78.5)	2,293 (91.4)*	9,795 (78.1)	3,730 (91.0)*	16,108 (78.6)	83 (96.5)*	298 (69.3)
Number of prescriptions, mean (SD) ^d	20.6 (22.1)*	18.7 (20.9)	21.2 (22.4)*	18.6 (21.8)	20.9 (22.2)*	18.7 (21.5)	24.2 (25.0)*	14.0 (15.4)
Patients with an iron chelator prescription, n (%)	17 (1.0)*	0	105 (4.2)*	0	58 (1.4)*	0	64 (74.4)*	0

^aP < 0.05. ^bAmong patients with event (visit/admission/prescription, etc.). ^cIncludes office visits, emergency room (ER) visits, laboratory services, physical therapy, occupational therapy, chiropractic services, transfusions, iron chelation therapy, magnetic resonance imaging (MRI), bone mineral density (BMD) tests. ER, emergency room; HCRU, healthcare resource utilization; NTDT, non-transfusion-dependent thalassemia; TDT, transfusion-dependent thalassemia.

- In the Commercial/Medicare population, healthcare costs (PPPY) during the 12-month follow-up were significantly higher across all thalassemia cohorts compared with matched controls (all P < 0.05; Figure 3).
- In the Medicaid population, healthcare costs (PPPY) were significantly higher across the α-thalassemia, β-thalassemia, and NTDT cohorts compared with matched controls (all P < 0.05; Supplemental Figure; see QR code).
 - Note: Sample sizes were low in TDT groups. Therefore, statistical comparisons were not conducted in TDT groups vs their matched controls.

During the variable length follow-up:

- Significantly more inpatient deaths occurred in all thalassemia patient cohorts compared with matched control groups (all P < 0.05) in the Commercial/Medicare population (Table 2).
- Significantly more inpatient deaths occurred in patients with α-thalassemia, β-thalassemia, and NTDT cohorts compared with matched control groups (all P < 0.05) in the Medicaid population (Table 2). No deaths occurred in the TDT patient group.
- No deaths occurred in any matched control group across both databases.

Table 2. Mortality in Commercial/Medicare and Medicaid Populations During Variable Length Follow-up

	Commercial/Medicare							
	α-Thalassemia (N = 1,628)	α-Thalassemia Control (N = 8,140)	β-Thalassemia (N = 2,449)	β-Thalassemia Control (N = 12,245)	NTDT (N = 4,097)	NTDT Control (N = 19,995)	TDT (N = 78)	TDT Control (N = 390)
Inpatient deaths, n (%)	8 (0.5)*	0 (0)	7 (0.3)*	0 (0)	13 (0.3)*	0 (0)	2 (2.6)*	0 (0)
Days follow-up, mean (SD)	1,132 (615)		1,080 (590)		1,101 (599)		1,091 (690)	
	Medicaid							
	α-Thalassemia (N = 559)	α-Thalassemia Control (N = 2,795)	β-Thalassemia (N = 739)	β-Thalassemia Control (N = 3,695)	NTDT (N = 1,289)	NTDT Control (N = 6,445)	TDT (N = 9)	TDT Control (N = 45)
Inpatient deaths, n (%)	7 (1.3)*	0 (0)	9 (1.2)*	0 (0)	16 (1.2)*	0 (0)	0 (0)	0 (0)
Days follow-up, mean (SD)	1,188 (660)		1,263 (694)		1,232 (680)		1,091 (796)	

^aP < 0.05.
 NTDT, non-transfusion-dependent thalassemia; TDT, transfusion-dependent thalassemia.

LIMITATIONS

- These analyses relied on diagnosis codes, procedure codes, and pharmacy prescriptions in health insurance claims, which are subject to data coding limitations and data entry error, to identify patient clinical profiles and study outcomes (no chart reviews were conducted).
- Only deaths that occurred in the inpatient setting were identified. Therefore, deaths are likely under-reported in this study.
- Some patients with thalassemia minor may have been coded incorrectly by physicians and thus included in the NTDT group, suggesting that NTDT estimates in this study may provide a lower boundary for the impact of NTDT on HCRU and economic burden.
- Sample sizes were low in both TDT groups.
 - The number of patients with TDT in the Merative™ MarketScan® Multi-State Medicaid Database was quite low; statistical comparisons were not conducted vs matched controls, and P values were not calculated.
 - TDT results from the Merative™ MarketScan® Commercial and Medicare Databases should be interpreted with caution.

CONCLUSIONS

- Patients with thalassemia, including those with α-thalassemia and NTDT, had significantly higher HCRU, total costs, and inpatient mortality rates than matched controls.
- Results are mostly consistent across the Commercial/Medicare and Medicaid patient populations.
- Alternative treatment options are needed to address the underlying pathophysiology of thalassemia to prevent serious complications and reduce HCRU.

ABBREVIATIONS: α, alpha; β, beta; BMD, bone mineral density; CPI, Consumer Price Index; ER, emergency room; HA, hemolytic anemia; HCRU, healthcare resource utilization; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; MRI, magnetic resonance imaging; NTDT, non-transfusion dependent thalassemia; OP, outpatient; PPPY, per person per year; TDT, transfusion dependent thalassemia; US, United States.

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SUPPLEMENTAL MATERIALS

