AAVBC

AMERICAN ACADEMY OF VALUE BASED CARE

Thalassemia

Quick Reference Guide

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1 CLINICAL SNAPSHOT

Definition: Thalassemia is a group of autosomal recessive hemoglobinopathies caused by defective synthesis of the alpha- or beta-globin chains of hemoglobin, producing chain imbalance, ineffective erythropoiesis, and chronic hemolytic anemia.[1] Severity spans a wide spectrum, so a single chart label of "thalassemia" can mean anything from an asymptomatic carrier to a patient in heart failure from decades of iron overload. Two axes define the condition: **alpha** (deletions of one to four **HBA1/HBA2** genes) versus **beta** (point mutations of the **HBB** gene), and carrier/trait versus clinically significant disease.[1] For management, the operative framework is **transfusion-dependent thalassemia (TDT)** versus **non-transfusion-dependent thalassemia (NTDT)** — the classification that drives transfusion protocol, chelation thresholds, monitoring frequency, and therapy eligibility. Thalassemia is best understood as a multisystem disease of iron overload, not simply as anemia: cardiac siderosis, endocrinopathy, hepatic fibrosis, and osteoporosis are the long-term drivers of morbidity, mortality, and cost.[2]

ICD-10 Codes:

Thalassemia is reported under the **D56** family, with subtype specificity directly determining risk-adjustment documentation. **D56.0** (alpha thalassemia) covers HbH disease (3-gene deletion); **D56.1** (beta thalassemia) covers both major/TDT and intermedia/NTDT; **D56.2** (delta-beta thalassemia); **D56.5** (hemoglobin E-beta thalassemia, common in Southeast Asian populations); **D56.8** (other thalassemias); and **D56.9** (thalassemia, unspecified). Trait and carrier states use **D56.3** (thalassemia minor) and **D56.4** (hereditary persistence of fetal hemoglobin) — neither maps to an HCC. Sickle-cell thalassemia is coded separately: **D57.42** (beta-zero without crisis) and **D57.44** (beta-plus without crisis). Iron overload is coded distinctly from the thalassemia itself — **E83.111** for hemochromatosis due to repeated transfusions (TDT) and **E83.118** for absorption-related overload (NTDT) — and other documentable complications include **I43** (cardiomyopathy), **K74.60** (cirrhosis), **C22.0** (hepatocellular carcinoma), **M81.0** (osteoporosis), **E03.9** (hypothyroidism), **E13.–** (secondary diabetes), and **F32.–/F41.–** (depression/anxiety). Document alpha-vs-beta, TDT-vs-NTDT status, and genetic-testing results to support the most specific code the record allows.[3]

Prevalence and Burden: Thalassemias are the most common monogenic disorders worldwide — roughly **1.5%** of the global population carries a beta-thalassemia allele and about **5%** an alpha-thalassemia allele, with more than **90%** of clinically affected patients living in a belt extending from the Mediterranean through the Middle East, Indian subcontinent, and Southeast Asia.[4] US data are sparse and rely on registry extrapolation: an estimated **11,262** patients have clinically significant thalassemia, a combined alpha- and beta-thalassemia prevalence of about **3.5 per 100,000**, and roughly **27%** of US thalassemia patients are foreign-born.[5,6] No published data describe thalassemia prevalence in Medicare or Medicare Advantage populations; patients surviving to age 65+ are a growing but poorly characterized cohort, the product of improved chelation and transfusion practice.[4,7]