

## Five-Year Fracture Rate for Transgender and Gender Diverse Patients on Gender-Affirming Hormone Therapy

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**Purpose:** Gender-affirming hormone therapy (GAHT) is a cornerstone of gender-affirming care for transgender and gender diverse (TGD) patients, with a direct biological role on bone metabolism. A paucity of data, however, describes how GAHT influences fracture rate over time. This study sought to describe the 5-year all-cause fracture incidence rate (IR) among TGD patients initiating estrogen-based (E-GAHT) or testosterone-based (T-GAHT) therapy, compared to TGD patients not using GAHT (non-GAHT).

**Methods:** This retrospective cohort study used commercial insurance data from the MarketScan Commercial Claims Database from January 1, 2009 to December 31, 2019 to identify TGD adults aged 18 to 65 years with evidence of E-GAHT or T-GAHT initiation or no evidence of GAHT use. The main outcome was incidence rate (IR with 95% confidence intervals [CI]) of all-cause fracture after up to 5 years of follow-up. The IR ratio (IRR) was estimated by comparing E-GAHT and T-GAHT groups to the non-GAHT group. Cox proportional hazards regression models estimated the hazard ratio (HR) after adjusting for age, comorbidity status using Charlson Comorbidity Index (CCI), presence of baseline fracture, and year of study start date.

**Results:** A cohort of 9696 TGD adults (E-GAHT [n = 1131]; T-GAHT [n = 1046]; non-GAHT [n = 7519]) was identified using clinical and enrollment criteria. The groups were similar in age (mean age [SD], 33.4 [13.2], 30.8 [11.7], and 33.2 [13.6], respectively) and CCI (percent with CCI = 0 [CCI = 3+]; 86.7% [2.2%], 84.9% [1.4%], and 85.3% [1.9%]). The IR of fracture was 13.9 (95% CI = 9.1-18.8) for E-GAHT, 15.3 (95% CI = 10.1-20.4) for T-GAHT, and 19.2 (95% CI = 16.9-21.4) for non-GAHT. Compared to non-GAHT, the crude IRR and fully-adjusted HR (aHR) was 0.73 (95% CI = 0.51-1.04) and 0.71 (95% CI = 0.49-1.02), respectively, for E-GAHT and 0.80 (95% CI = 0.56-1.14) and 0.78 (95% CI = 0.55-1.12), respectively, for T-GAHT.

**Conclusion:** The 5-year incidence of all-cause fracture was lower for TGD adults initiating E-GAHT and T-GAHT when compared to non-GAHT upon analysis of a commercial claims database, but the difference was not statistically significant. These results provide reassurance that GAHT use is not negatively associated with 5-year all-cause fracture rate.