

# Impact of Reference Gender on Bone Mineral Density and Fracture Risk Assessment in Transgender Adults



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## BACKGROUND

Bone health in transgender people is influenced by hormonal, metabolic, and behavioral factors. Before starting gender-affirming hormone therapy (GAHT), people assigned male at birth (AMAB) often show reduced bone mineral density (BMD) for age, while data for those assigned female at birth (AFAB) are conflicting. Guidelines for assessing osteo-metabolic risk in the transgender population are still evolving, particularly regarding the choice of reference gender in densitometry or fracture risk calculators.

## AIM

To evaluate the impact of reference gender on BMD assessment and fracture risk scores in transgender people naïve to GAHT. Secondary objectives included determining the prevalence of reduced BMD for age and exploring correlations with clinical, hormonal, and metabolic factors.

## MATERIALS AND METHODS

Participants were enrolled among transgender individuals, aged <50 years, evaluated before GAHT at the Hospitals of Padua and Brescia (Italy) between 2021-2025. Clinical, anthropometric, and biochemical data, including vitamin D and sex hormones, were collected. BMD was measured by Hologic DXA at lumbar and femoral sites. Z scores were calculated using the same set of reference data, both for male and female reference populations. Fracture risk was assessed with the FRAX algorithm, calculated for both genders; individuals between 18-40 years were entered as 40 years old, corresponding to the minimum valid age. FRAX was considered elevated: >20% for major fractures and >3% for hip fractures.

## RESULTS

We recruited **249 transgender individuals** (153 AFAB, 96 AMAB), aged 18-43 years (median age 23 years), with a median BMI of 22.0 kg/m<sup>2</sup>. Most participants were Caucasian (96.8%).

At baseline, **no fragility fractures** were reported. However, 40 individuals (16.1%) presented at least one relevant osteo-metabolic risk factor. The most frequent was **underweight**, observed in 33 cases. No case of hypogonadism was observed. Overall, **66.7%** of participants showed **vitamin D deficiency** (<50 nmol/L).

Differences in Z-scores and FRAX values are presented in Table 1. In both groups, Z-scores were significantly lower when calculated using the male reference database ( $\Delta Z \approx 0.4-0.6$ ). Overall, switching from the female to the male reference altered BMD classification (Z >-1; Z -1;-2; Z <-2) in 32.2% of AFAB and 26.0% of AMAB individuals.

**AMAB individuals** more frequently presented **low BMD for age** compared with AFAB individuals (**11.5% vs 3.9%** using the female reference, and **27.1% vs 13.7%** using the male reference, respectively). Despite these differences, FRAX estimates remained low in both groups; only one AMAB participant met criteria for elevated hip fracture risk.

AFAB	Female reference	Male reference	P-value
Z-score L1L4	+0,01 (-0,75 – +0,68)	-0,52 (-1,23 – +0,14)	<0,0001
Z-score F tot	-0,14 (-0,90 – +0,57)	-0,82 (-1,39 – -0,17)	<0,0001
Z-score F neck	-0,25 (-1,05 – +0,47)	-0,79 (-1,47 – -0,22)	<0,0001
Low BMD (Z ≤ -2)	6 (3,9%)	21 (13,7%)	<0,0001
Z-score: -1; -2	46 (30,1%)	65 (42,8%)	<0,0001
FRAX major fr. (%)	1,8 (1,7 - 2,1)	1,8 (1,6 - 2,4)	<0,0001
FRAX hip fr. (%)	0,1 (0,0 - 0,2)	0,1 (0,1 - 0,4)	<0,0001

  

AMAB	Female reference	Male reference	P-value
Z-score L1L4	-0,42 (-1,20 – +0,53)	-0,83 (-1,73 – -0,04)	<0,0001
Z-score F tot	-0,15 (-1,20 – +0,53)	-0,78 (-1,63 – -0,18)	<0,0001
Z-score F neck	-0,21 (-1,12 – +0,67)	-0,80 (-1,51 – -0,05)	<0,0001
Low BMD (Z ≤ -2)	11 (11,5%)	26 (27,1%)	0,002
Z-score -1; -2	34 (35,4%)	29 (30,2%)	0,002
FRAX major fr. (%)	1,8 (1,6 - 2,2)	1,9 (1,6 - 2,4)	<0,0001
FRAX hip fr. (%)	0,1 (0,0 - 0,2)	0,2 (0,1 - 0,4)	<0,0001

**Table 1.** Description of densitometric and FRAX score data in the transgender AFAB and AMAB samples.

## Factors associated with reduced BMD

In AFAB individuals, **BMI** showed a significant association ( $p < 0.0001$ ) with bone density status. Spearman's correlation confirmed the protective role of BMI on bone density and FRAX scores.

In AMAB individuals, BMD, Z-scores and FRAX values were associated with **BMI and vitamin D**. A correlation between BMI, vitamin D and estradiol levels with BMD, Z-scores, and FRAX for hip fractures as found. Lastly, a multivariate linear regression. Revealed that BMI and vitamin D were independent predictors of BMD and Z-score for AMAB individuals

## CONCLUSIONS

The choice of reference gender significantly influences densitometric interpretation in young transgender adults. Until population-specific normative data become available, calculating Z-scores using both male and female reference databases is advisable. Early preventive interventions remain essential to preserve bone health.