

Long term effects of treatment with Oxandrolone in addition to growth hormone in girls with Turner syndrome on bone mineral density in adulthood

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Introduction

Low dose Oxandrolone (Ox) in addition to growth hormone (GH) treatment increases adult height in Turner Syndrome (TS) more than GH alone. However, the effects of Ox in childhood on bone mineral density (BMD) in adulthood are unknown.

Conclusions

Adults with TS treated with GH in childhood have a lower BMD than healthy individuals of the same age.

The addition of Ox to GH in childhood results in a significantly higher lumbar spine BMD in adulthood than GH alone, with a similar trend for the femoral neck and total body, without significant dosage differences.

Study design

During the previous randomised controlled trial, 133 girls were treated with GH plus placebo (PI), Ox 0.03, or Ox 0.06 mg/kg/day from 8 years of age and estrogens from 12 years of age. Sixty-six women (PI, n=21; Ox 0.03, n=27; Ox 0.06, n=18) participated in the double-blind follow-up study (mean age 24.0±7.6 yr; mean time since stopping GH, 9.0±3.1 yr; and mean time of Ox/PI use 5.0±3.0 yr). BMD of the lumbar spine (LS), femoral neck (FN) and total body (TB) were assessed using DXA Hologic.

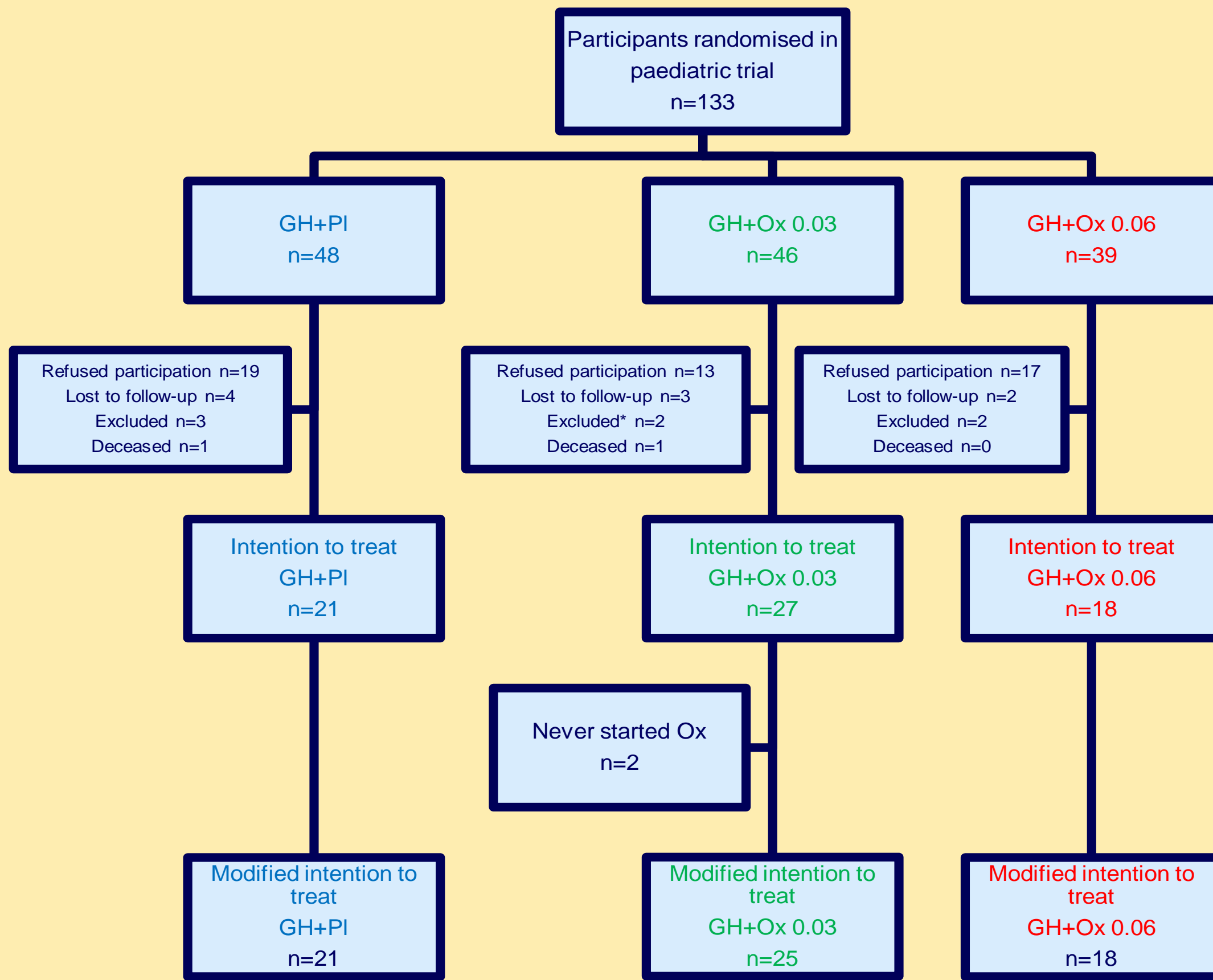


Figure 1 Follow-up of participants in the original study and inclusion to the current study.

Patient characteristics

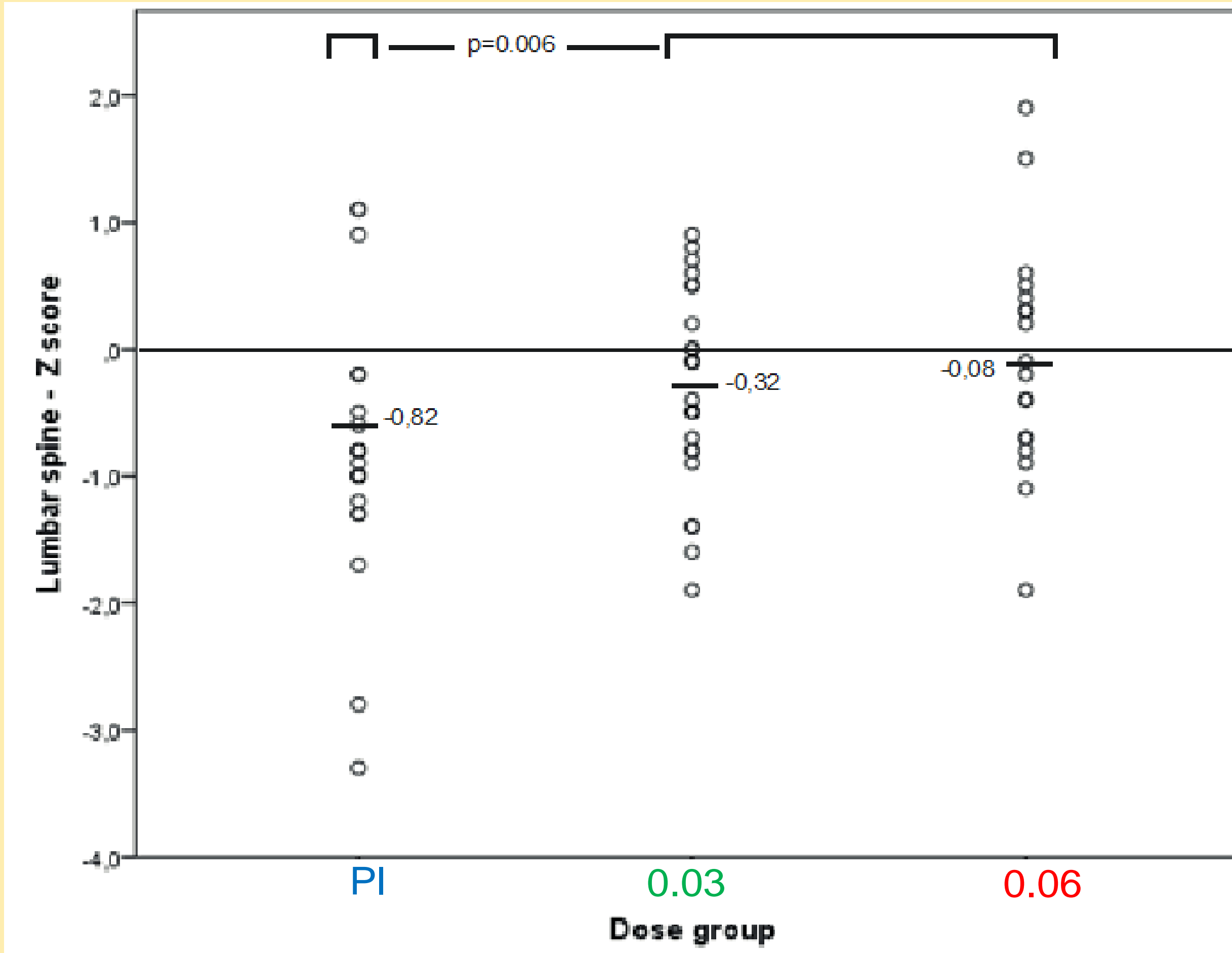
Table 1 Patient characteristics of patients treated with growth hormone (GH) and placebo (PI), Oxandrolone (Ox) 0.03 or 0.06 mg/kg/day of the intention to treat group

	GH+PI (n=21)	GH+Ox 0.03 (n=27)	GH+Ox 0.03 vs GH+PI, p-value	GH+Ox 0.06 (n=18)	GH+Ox 0.06 vs GH+PI, p-value
Age (yr)	24.4±4.3	23.8±3.7	0.800	23.7±3.4	0.561
Karyotype 45,X (%)	12/21 (57.1)	10/27 (37.0)	0.380	8/18 (44.4)	0.380
Age start GH (yr)	9.5±3.7	9.0±3.8	0.456	8.6±3.0	0.400
Age start Ox/PI (yr)	10.5±2.4	10.4±2.2 ^a	0.921	9.7±1.7	0.265
Duration GH (yr)	6.0±2.7 ^b	6.2±3.4	0.799	6.2±2.3	0.782
Duration Ox/PI (yr)	5.3±1.6	4.7±1.5	0.221	5.0±1.3	0.514
pt using of HRT (%)	18 (85.7)	22 (81.5)	0.927	15 (83.3)	0.927
Age start E2 (yr) ^c	13.2±1.5	13.0±1.1	0.661	12.6±0.8	0.207

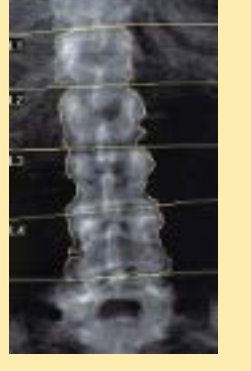
- Two participants never started oxandrolone therapy, both in Ox 0.03 group.
- One participant in the PI group had not yet terminated GH and OX therapy at the follow-up moment.
- Only participants using estrogens.

Results

Characteristics of included patients in this follow-up study were comparable with the non-participants (treated only in the original study in childhood). Only duration of Ox therapy was 0.9 year longer in participants compared with non-participants. BMD z-scores in the PI group were significantly lower than zero.



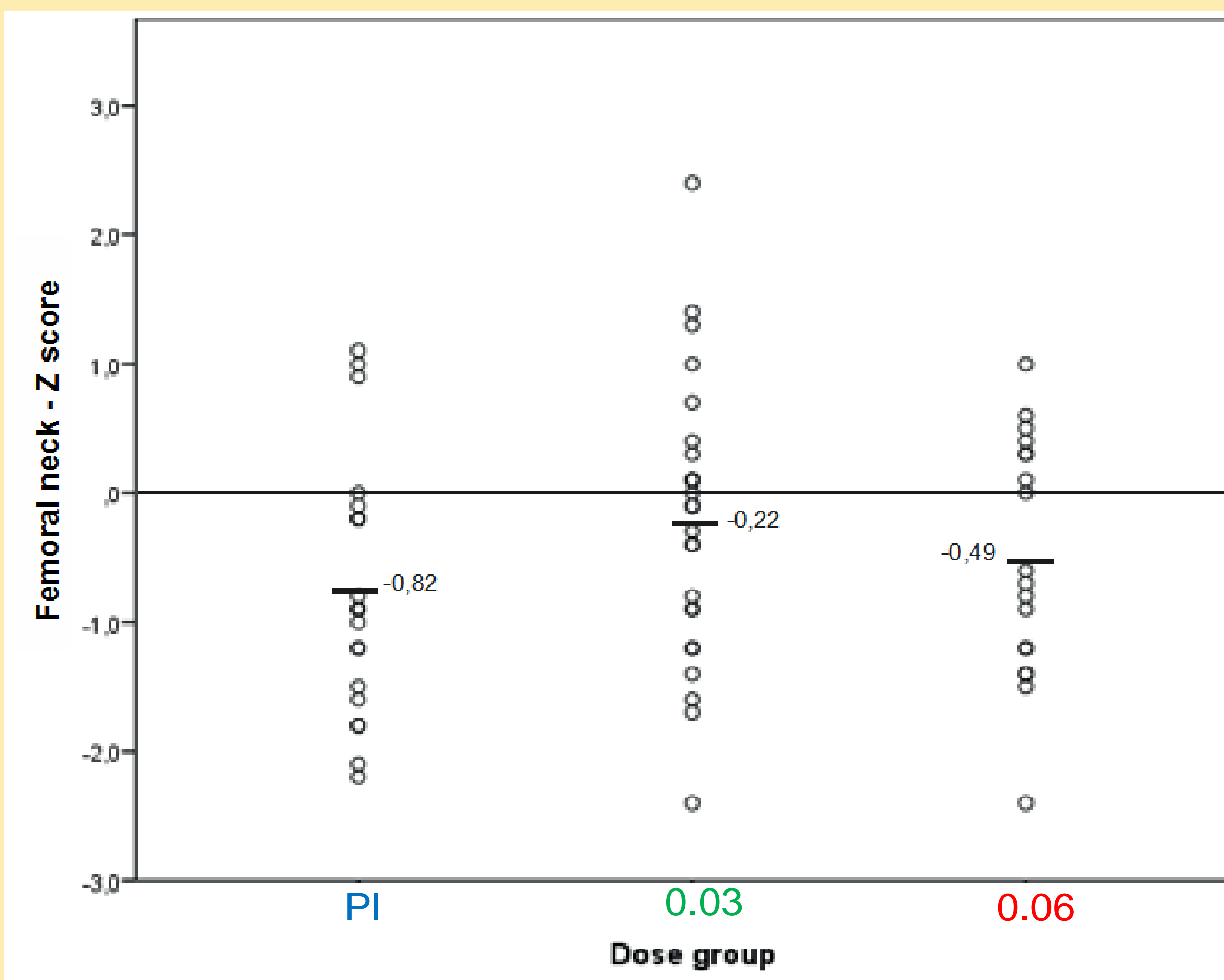
Lumbar spine



BMD Z-score of the lumbar spine was higher in the Ox groups (0.03 and 0.06) than in the PI group (p-value 0.006), even after adjustment for height or adjustment for height and duration of Ox treatment.

The difference between the 0.03 and 0.06 was not statistically significant.

BMAD using 17 yr Hologic references shows similar results.

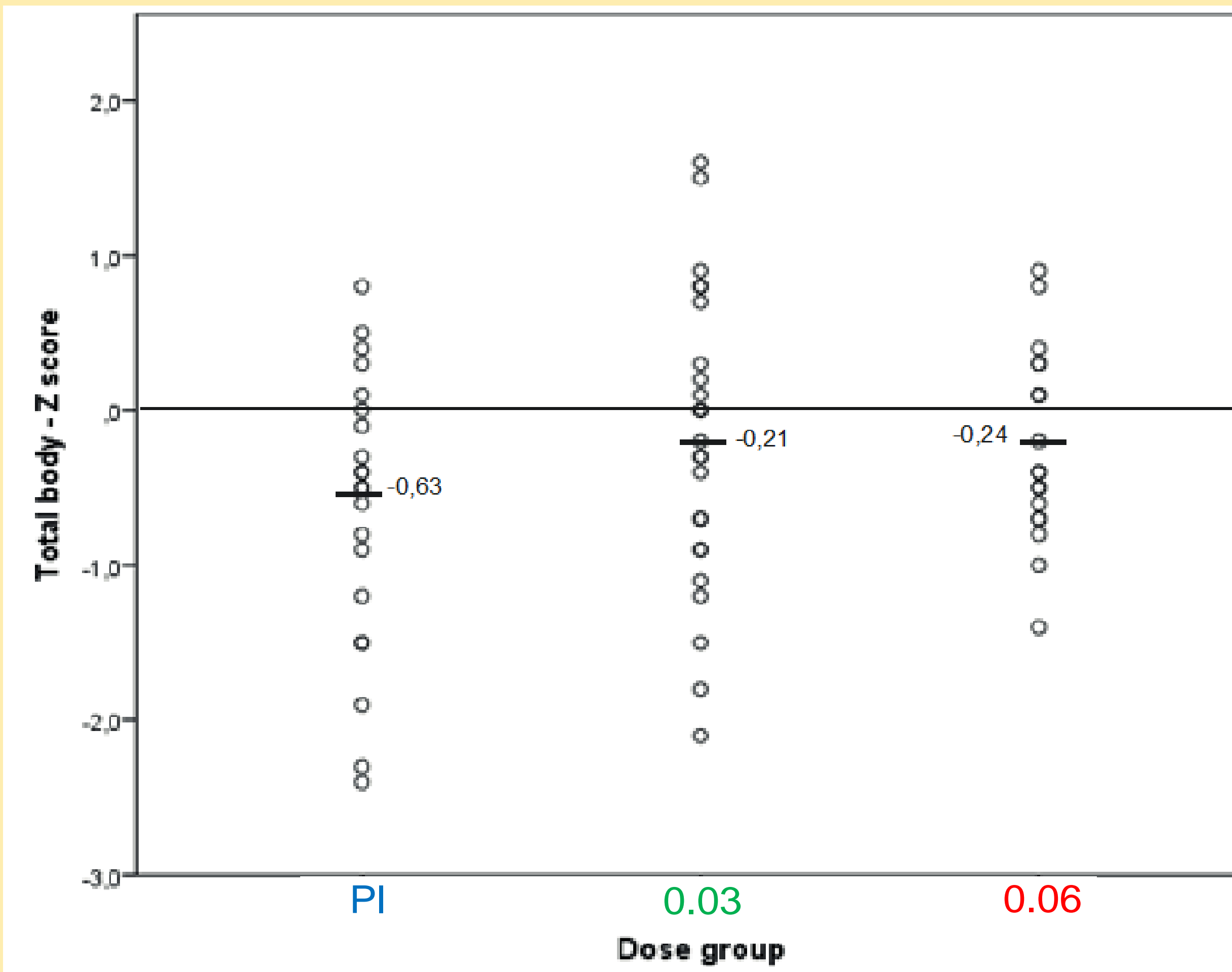


Femoral neck



Although there is a trend towards higher BMD Z-score of the femoral neck in the Ox groups (0.03 and 0.06) than in the PI group, the differences were not statistically significant.

BMAD using 17 yr Hologic references shows similar results.



Total body



Although there is a trend towards higher BMD Z-score of the total body in the Ox groups (0.03 and 0.06) than in the PI group the differences were not statistically significant.

BMAD using 17 yr Hologic references shows similar results.

Limitations

- No DXA BMD measurements were done during childhood or at end of the initial study.
- Only half of the original participants could be included for the follow-up. However the number of dropouts was almost equally distributed among the treatment arms, suggesting that the sample remains representative of the cohort.
- BMD may appear falsely reduced when evaluated by DXA due to the small bone size accompanying short stature and the differences in bone geometry due to SHOX deficiency. However, we made adjustments for height and we calculated BMAD.

References

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Growth and syndromes (to include Turner syndrome)
Theo Sas

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