

Letter to the Editor

Optimal Thresholds, Linear or Nonlinear Relationships of Fracture Risk Reduction With Therapy

To the Editor:

We read with interest the response by Dr Eastell et al.⁽¹⁾ regarding the reanalysis of his 2003 *JBMR* paper.⁽²⁾ The allegations that the study sponsor withheld data and did not allow all authors full access to the raw data are serious and clearly deserve a detailed response. However, the reanalysis raises a number of issues. We commend the authors for supplementing the smoothed curves with decile analyses but are mystified why Tables 1 and 2 in the response show incident vertebral fracture rates from the risedronate and placebo groups combined, because the decile cut-points for the two treatment groups must differ, and the relationship between change in bone turnover and fracture in the placebo group is not relevant. Even if a statistically significant interaction with treatment group assignment is not found, the decile analyses of the risedronate and placebo groups should be displayed and analyzed separately (as alluded to in the Appendix). Inferences about optimal thresholds and nonlinear relationships, including the statements that critical thresholds were observed at a “CTX reduction of 51%” and at an on-therapy “CTX T-score of 0,” may be incorrect if derived from pooled risedronate and placebo group data. This issue is particularly concerning given that, among risedronate-treated women, only 36 suffered a new vertebral fracture.⁽²⁾ Furthermore, no data are presented to support the statement in the Appendix that on-therapy measurement of bone turnover is “a better measure of future fracture” than short-term changes in bone turnover. As pointed out in the accompanying Editorial,⁽³⁾ it is unfortunate that the authors of the response did not comment on the ob-

served inconsistencies between their revised N-terminal cross-linking telopeptide of type I collagen (NTX) and C-terminal cross-linking telopeptide of type I collagen (CTX) results, nor do they describe any reanalysis of nonspine fracture data. Last, we believe that the results of the revised analyses should be considered in the context of more recent data from larger antiresorptive trials that do not support a nonlinear relationship between short-term changes in bone turnover and subsequent fracture incidence.^(4,5)

REFERENCES

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